VOLUME 80 • AUGUST 1959 • NUMBER 2

A.M.A. ARCHIVES OF

DERMATOLOGY

Bowen's Disease and Its Relationship to Systemic Cancer
James H. Graham and Elson B. Helwig

Epidermal Changes Associated with Sclerosing Hemangiomas
Hillard J. Halpryn and Arthur C. Allen

Monoporous and Polyporous Acne
John B. Watson

The History of Dermatology as Depicted on Postage Stamps
Samuel M. Bluefarb

The Treatment of Scleroderma with the New Chelating Agent, Edathamil
Sigfrid A. Muller, Louis A. Brunsting, and R. K. Winkelmann

Idiopathic Atrophoderma of Pasini and Pierini Occurring in Two Brothers
Marc Allen Weiner and James Q. Gant Jr.

Dexamethasone in Dermatology
Norman B. Kanof and Saul Blau

Ringworm of the Scalp in the Delta of the Rio Grande
Ivan W. Kuhl

Erythromycin in the Treatment of Early Syphilis
C. Hunter Montgomery and John M. Knox

The Psoriatic Process
Daphne Anderson Roe

Double-Blind Evaluation of Trimeprazine
Irving D. London

Ingrown Hairs of the Bearded Areas of the Face and Neck
C. Russell Anderson

A New Phenolated Scalp Oil
Leon Goldman and Robert H. Preston

Partial Alopecia Due to Thallium
W. R. Hubler

A New Shampoo for Seborrheic Dermatitis
Leonard V. Kornblee, Arthur H. Gladstein, and Paul Lazar

Azure Lunulae
Irving L. Leff

A Technique for Intravenous Therapy in Patients with Scleroderma and in Apprehensive Children
John S. Lundy

Removal of Linear Scars
John J. McAndrew

Onset of Psoriasis During the Course of Steroid Therapy
Samuel J. Zakon and Fred Levit

Nail Changes Due to New Base Coat
Milton Reisch

Obituary: Lester Hollander, M.D.

The New, Newer, and Newest

Bronx Dermatological Society

Detroit Dermatological Society

Los Angeles Dermatological Society

Manhattan Dermatological Society

Metropolitan Dermatological Society of New York

Announcements

Books

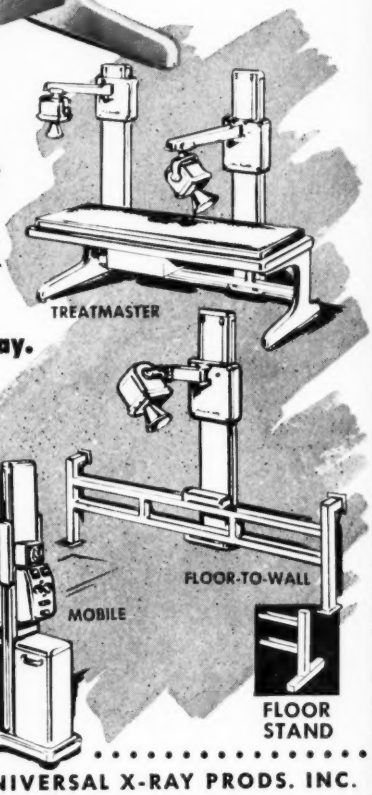
AMERICAN MEDICAL ASSOCIATION PUBLICATION

TREATMASTER

GRENZ RAY THERAPY UNITS

by UNIVERSAL

Manufacturers of fine equipment for over 30 years



A wide variety of models in either X-Ray or Grenz Ray.

Universal skin therapy X-Ray and Grenz Ray units are available in a variety of models to suit most any type of office layout. Any model you choose has the same high standards of craftsmanship and unique advantages that has made the Universal skin therapy line so outstanding among the many leading dermatologists, hospitals and clinics throughout the world.

- **High output—desirable quality of radiation**
- **Simple and convenient handling**
- **Safety in everything from lead shielding to electrical and mechanical construction**
- **Priced within the reach of even the doctor just starting practice**

You owe it to yourself to investigate

SEND NOW FOR FREE TECHNICAL DATA

UNIVERSAL X-RAY PRODS. INC.

1140 N. Western Ave. • Chicago 22, Ill. • U. S. A.

Please mail more detailed prices and information on:

☐ X-Ray Therapy ☐ Grenz Ray Therapy

Doctor_____

Address _____

City_____ State_____

TABLE OF CONTENTS

VOLUME 80 AUGUST 1959 NUMBER 2

ORIGINAL ARTICLES

PAGE

Bowen's Disease and Its Relationship to Systemic Cancer
James H. Graham, M.D., and Elson B. Helwig, M.D., Washington, D. C. 133

Epidermal Changes Associated with Sclerosing Hemangiomas
Hillard J. Halpryn, M.D., and Arthur C. Allen, M.D., Miami, Fla. 160

Monoporous and Polyporous Acne
John B. Watson, M.D., Hollywood, Calif. 167

The History of Dermatology as Depicted on Postage Stamps
Samuel M. Bluefarb, M.D., Chicago 171

The Treatment of Scleroderma with the New Chelating Agent, Edathamil
Sigfrid A. Muller, M.D.; Louis A. Brunsting, M.D., and R. K. Winkelmann, M.D., Rochester, Minn. 187

Idiopathic Atrophoderma of Pasini and Pierini Occurring in Two Brothers
Marc Allen Weiner, M.D., and James Q. Gant Jr., M.D., Washington, D.C. 195

Dexamethasone in Dermatology
Norman B. Kanof, M.D., and Saul Blau, M.D., New York 198

Ringworm of the Scalp in the Delta of the Rio Grande
Ivan W. Kuhl, M.D., McAllen, Texas 202

Erythromycin in the Treatment of Early Syphilis
C. Hunter Montgomery, M.D., and John M. Knox, M.D., Houston, Texas 205

The Psoriatic Process
Daphne Anderson Roe, M.D., M.R.C.P., Wilmington, Del. 210

CLINICAL NOTES, NEW INSTRUMENTS AND TECHNIQUES

Double-Blind Evaluation of Trimeprazine
Irving D. London, M.D., Montgomery, Ala. 220

Ingrown Hairs of the Bearded Areas of the Face and Neck
C. Russell Anderson, M.D., Beverly Hills, Calif. 222

A New Phenolated Scalp Oil
Leon Goldman, M.D., and Robert H. Preston, M.D., Cincinnati 222

Partial Alopecia Due to Thallium
W. R. Hubler, M.D., Corpus Christi, Texas 223

A New Shampoo for Seborrheic Dermatitis
Leonard V. Kornblee, M.D., New York; Arthur H. Gladstein, M.D., Astoria, N. Y., and Paul Lazar, M.D., Chicago 223

Azure Lunulae
Irving L. Leff, M.D., Buffalo 224

A Technique for Intravenous Therapy in Patients with Scleroderma and in Apprehensive Children
John S. Lundy, M.D., Rochester, Minn. 226

Removal of Linear Scars
John J. McAndrew, M.D., Orlando, Fla. 227

Onset of Psoriasis During the Course of Steroid Therapy
Samuel J. Zakon, M.D., and Fred Levit, M.D., Chicago 229

Nail Changes Due to New Base Coat
Milton Reisch, M.D., New York 230

OBITUARIES

Lester Hollander, M. D. 232

THE NEW, NEWER, AND NEWEST 235

SOCIETY TRANSACTIONS

Bronx Dermatological Society 238
Detroit Dermatological Society 248
Los Angeles Dermatological Society 250
Manhattan Dermatological Society 253
Metropolitan Dermatological Society of New York 256

REGULAR DEPARTMENTS

Announcements 234, 237
Books 258

A. M. A.
ARCHIVES OF DERMATOLOGY

VOLUME 80 AUGUST 1959 NUMBER 2

Copyright, 1959, by the AMERICAN MEDICAL ASSOCIATION
Published under the Auspices of the Board of Trustees

EDITORIAL BOARD

HERBERT RATTNER, Chief Editor
104 South Michigan Avenue, Chicago 3

HARVEY BLANK, Miami, Fla.
LOUIS BRUNSTING, Rochester, Minn.
J. LAMAR CALLAWAY, Durham, N. C.
A. C. CIPOLLARO, New York
GEORGE M. LEWIS, New York
H. E. MICHELSON, Minneapolis

J. F. HAMMOND, Editor, A. M. A. Scientific Publications
GILBERT S. COOPER, Managing Editor, Specialty Journals
T. F. RICH, Assistant Managing Editor, Specialty Journals

The A. M. A. Archives of Dermatology is published monthly by the American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois, and is an official publication of the Association.

Executive Vice President: F. J. L. BLASINGAME, M.D.
Business Manager: RUSSELL H. CLARK

ADVERTISING: Business Director, Russell H. Clark; Advertising Production Manager, Walter H. Kimotek. Advertising Representatives: Vernon J. Wendt, 535 North Dearborn Street, Chicago 10, Illinois, WHitehall 4-1500; Al Detwiller, 475 Fifth Avenue—Room 1005, New York 17, New York, ORegon 9-9383; Dale B. Clarke, 1919 Wilshire Blvd., Los Angeles 57, California, HUbbard 3-3811.

CIRCULATION: Circulation Manager, Robert A. Enlow; Assistant Circulation Manager, Bernard F. Kroeger. The yearly subscription rate of the Archives of Dermatology is: U. S. and Possessions, $12.00; Canada, $12.50. Other Foreign Countries, $13.50. Single copies of this and previous calendar year, $1.25.

Back issues older that two years are available through Walter J. Johnson, Inc., 111 Fifth Avenue, New York 3, New York. Reprints of back issues available through Johnson Reprint Corporation, 111 Fifth Avenue, New York 3, New York.

CHANGE OF ADDRESS: Please notify publisher at least six weeks in advance, including both old and new address, and mailing label taken from the most recent copy. Include your new Postal Zone number, if you live in a zoned city.

Second-class postage paid in Nashville, Tennessee.

Please address communications and subscription orders to: American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois.

in
infected &
inflammatory
dermatoses

CHYMAR® ointment

CLEANS THE LESION Necrotic tissue, crusts, pyogenic membrane and exudates are cleared away through proteolytic action to expose the infected surface to the full effects of the antibiotic and anti-inflammatory agents in Chymar Ointment . . . odors are prevented or counteracted . . . healing is helped . . . scar formation lessened.

CLEARS INFECTION Both gram-negative and gram-positive bacteria and some fungi are sensitive to neomycin palmitate. Infection is brought under control quickly, further invasion by pathogens is prevented, no bacterial resistance is produced, sensitivity is rare.

CONTROLS INFLAMMATION Chymar Ointment reduces erythema, edema and pruritus without systemic effects and with no interference with healing. It keeps the patient more comfortable while infection heals . . . helps prevent spread of infection through scratching . . . produces no corticosteroid side effects.

Each gram contains: Proteolytic Activity (provided by a concentrate of proteolytic enzymes from the pancreas, e.g. chymotrypsin and trypsin) 10,000 Armour Units; Neomycin Palmitate (as base) 3.5 mg.; Hydrocortamate HCl, 1.25 mg.; in a water-miscible base that permits full release of medicaments for fullest therapeutic benefit.

In contact, infectious, seborrheic or stasis dermatitis; infected neurodermatitis; psoriasis; impetigo; 2nd and 3rd degree burns; pustular lesions; ulcers (decubitus, cautery, varicose).

ARMOUR PHARMACEUTICAL COMPANY
KANKAKEE, ILLINOIS *Armour Means Protection*

Instructions to Contributors

Articles, book reviews, and other materials for publication should be addressed to the Chief Editor. Articles are accepted for publication on condition that they are contributed solely to this journal.

An original typescript of an article, with one carbon copy, should be provided; it must be double or triple spaced on one side of a standard size page, with at least a 1-inch margin at each edge. Another carbon copy should be retained by the author.

The main title of an article may not contain more than eighty characters and spaces; a subtitle may be of any length.

The author's name should be accompanied by the highest earned academic or medical degree which he holds. If academic connections are given for one author of an article, such connections must be given for all other authors of the article who have such connections.

If it is necessary to publish a recognizable photograph of a person, the author should notify the publisher that permission to publish has been obtained from the subject himself if an adult, or from the parents or guardian if a child. An illustration that has been published in another publication should be accompanied by a statement that permission for reproduction has been obtained from the author and the original publisher.

Oversized original illustrations should be photographed and a print on glossy paper submitted. Prints of a bluish tinge should be avoided. Large photomicrograph prints will be reduced in scale unless portions to be cropped are indicated by the author. The author should submit duplicate prints of roentgenograms and photomicrographs with the essential parts that are to be emphasized circled, as a guide to the photoengraver.

Charts and drawings should be in black ink on hard, white paper. Lettering should be large enough, uniform, and sharp enough to permit necessary reduction. Glossy prints of x-rays are requested. Paper clips should not be used on prints, since their mark shows in reproduction, as does writing on the back of prints with hard lead pencil or stiff pen. Labels should be prepared and pasted to the back of each illustration showing its number, the author's name, and an abbreviated title of the article, and plainly indicating the top. Charts and illustrations must have descriptive legends, grouped on a separate sheet. Tables must have captions. ILLUSTRATIONS SHOULD BE UNMOUNTED.

References to the literature should be limited to those used by the author in preparation of the article. They should be typed on a special page at the end of the manuscript. The citation should include, in the order given, name of author, title of article (with subtitle), name of periodical, with volume, page, month—day of month if weekly or biweekly—and year. References to books must contain, in the order given, name of author, title of book, city of publication, name of publisher, and year of publication.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street **Chicago 10**

wherever the 4 winds blow

new 4 mg.

POLARAMINE®

dextro-chlorpheniramine maleate

REPETABS®

For day-to-day relief and maintenance in allergic reactions with these 4 major benefits

High degree of antihistamine efficacy—daylong or nightlong protection with a single 4 mg. REPETAB / Low dosage—lower than with other antihistamines / High therapeutic index (3380)—unsurpassed among all antihistamines / Low incidence of side effects—unexcelled by any other antihistamine preparation

4 mg. POLARAMINE REPETABS in bottles of 100 and 1000

SYMBOL OF THE ONE-DOSE CONVENIENCE YOU WANT FOR YOUR PATIENT.

• PROMPT REPETAB RELIEF • LASTS ALL DAY OR NIGHT •

Schering

HERING CORPORATION • BLOOMFIELD, N. J. EN1482-9

Never before in **ACNE!**

Graded long-term abrasion

The 3 grades of BRĀSIVOL permit a logical 3-step course of therapy:

1

Mild abrasion for 2-4 weeks with BRĀSIVOL FINE

2

More vigorous abrasion for 2-4 weeks with BRĀSIVOL MEDIUM

3

Maintenance treatment for as long as needed with BRĀSIVOL ROUGH

BRASIVOL introduces a new concept in the treatment of acne: prolonged superficial abrasion precisely adjustable to the patient's progress. Ten years of clinical studies in over a thousand acne patients have demonstrated the success of continuous abrasion in maintaining patency of the sebaceous ducts by gentle desquamation, thereby reducing comedones, papules, pustules and cysts, and minimizing post-acne scarring.

BRASIVOL contains non-silicon abrasives (fused synthetic aluminum oxide) of carefully selected particle sizes and in appropriate ratios, with hexachlorophene 1.0%, in a specially formulated base of soap and synthetic detergent.

1. Saperstein, R. B.: Presented at 107th annual meeting of American Medical Assn., San Francisco, Calif., June 23-27. 1958.

SUPPLIED:
Jars of Brāsivol Fine 6 oz.; Brāsivol Medium 6½ oz.; Brāsivol Rough 7 oz.

Brāsivol™

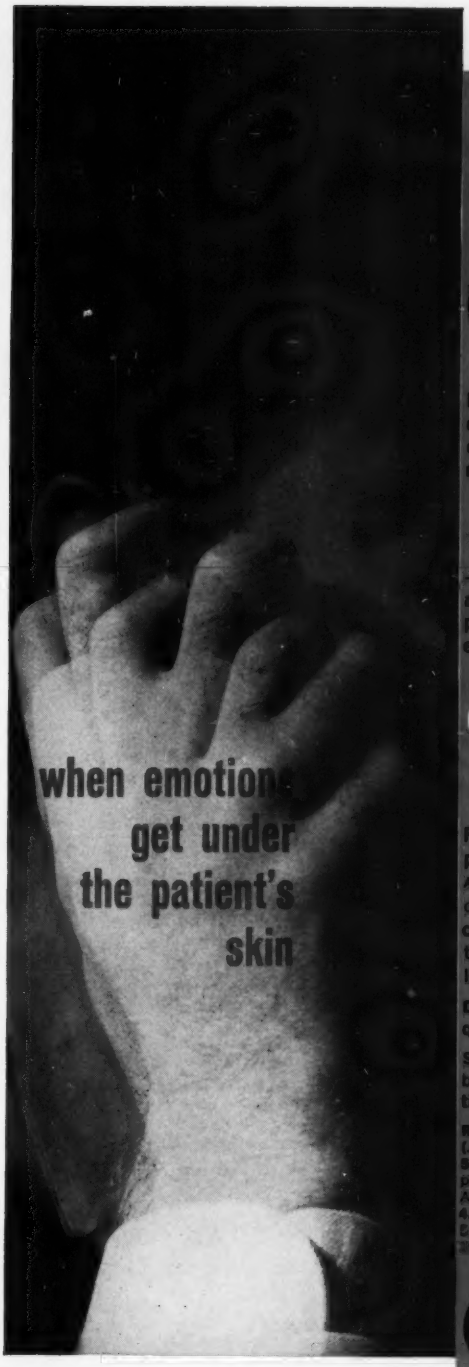
GRADED ABRASIVE CLEANSER FOR ACNE

Write for samples and informational literature

STIEFEL LABORATORIES, INC.
Oak Hill, New York

Canadian representatives:
WINLEY-MORRIS CO., LTD., Montreal 29, Quebec

FOUNDED 1847 STIEFEL®



A TRANQUILIZER UNIQUE
IN DERMATOLOGIC PRACTICE

dermatoses respond to

the calming action

Feinberg: "Tranquilizing drugs in general have an equivocal effect on the manifestations of allergic disease. . . . ATARAX may be one exception to the rule. . . ."[1]

and the anti-allergic effect

—Added antihistaminic action of ATARAX controls a wide variety of dermatological exacerbations: pruritus, urticaria, dermatitis, and other cutaneous eruptions.[2,3,4,5]

# of ATARAX

Feinberg[1] obtained "most striking results" in 17 patients with chronic urticaria. The effect of ATARAX was excellent in 15, fair to good in 2. After objective evaluation of 140 patients, Robinson[6] concludes that ATARAX is "valuable adjunctive therapy" for patients whose dermatoses are related to emotional tension.

Dosage: Adults, one 25 mg. tablet, or one tbsp. Syrup q.i.d. Children, 1 or 2 tsp. Syrup t.i.d.

Supplied: Tiny 10 mg., 25 mg., and 100 mg. tablets, bottles of 100. Syrup, pint bottles. Parenteral Solution, 10 cc. multiple-dose vials.

References: 1. Feinberg, A. R., et al.: J. Allergy 29:358 (July) 1958. 2. Robinson, H. M., Jr., et al.: South. M. J. 50:1282 (Oct.) 1957. 3. Santos, I. M., and Ungar, L.: Paper presented at 14th Annual Congress, American College of Allergists, Atlantic City, New Jersey, April 23-25, 1958. 4. Colrsurt, M., et al.: Presse méd. 64:2239 (Dec. 26) 1956. 5. Robinson, H. J., Jr., et al.: J.A.M.A. 161:604 (June 16) 1956.

FOBRIG

New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being

these physical scars need never have developed

Surgical techniques can now almost completely remove this man's severe acne scars. But if he, and thousands like him, had sought early treatment, the scars might never have developed. A physician's advice and guidance concerning his condition, plus treatment with 'Acnomel', might have prevented his acne from progressing to the severe, scarring stage.

'Acnomel' conceals acne lesions as it heals them, thus reducing embarrassment while treatment goes on. The results from 'Acnomel' therapy are often evident in a few days rather than in weeks or months.

When you see a patient who needs advice about acne, remember 'Acnomel'. Available in 2 forms: Cream for use at home; Cake in a handy compact for use away from home.

Acnomel* **conceals as it heals**

sulfur • resorcinol • hexachlorophene

Smith Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off.

TO TREAT

ITCHY, SCALY SCALP

WHICH TENDS TO DRYNESS

sebulex®

ANTISEBORRHEIC SHAMPOO

WESTWOOD PHARMACEUTICALS, Buffalo 13, New York

sebulex®

a therapeutic shampoo
for the treatment of itchy, scaly scalp
which tends to dryness

Stops itching, removes loose dandruff and crusty, matted layers of scales from the scalp through the effective cleansing, penetrating and antiseborrheic actions of *Sebulytic*®, a combination of anionic surface-active cleansers and wetting agents. The antiseborrheic qualities of Sebulytic are further enhanced with the addition of sulfur and salicylic acid. Hexachlorophene provides antibacterial action.

Prevents excessive drying of the scalp through the action of *Kerohydric*™, a crystal-clear, dewaxed fraction derived from lanolin. Kerohydric also leaves the hair soft and more manageable after shampooing.

Sebulex is cosmetically elegant. Sebulex meets the up-to-date "cosmetic" requirements for a therapeutic shampoo. It has a smooth, lotion-like texture, an appealing pastel green color, delightful fragrance and produces an abundant lather. Patients like shampooing with Sebulex.

Sebulex does not contain any toxic metallic materials. Thus, it can be used for a prolonged period of time without danger of systemic toxic effects.

Sebulex contains a mixture of anionic surface-active cleansers and wetting agents (Sebulytic). These agents consist of sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate, and sodium dioctyl sulfosuccinate. Sebulex also contains Kerohydric, a crystal-clear, dewaxed fraction of lanolin; sulfur 2%, salicylic acid 2% and hexachlorophene 1%.

Available: In plastic bottles of 4 oz. *Write for samples.*

WESTWOOD PHARMACEUTICALS, Buffalo 13, New York

now
in

POCKET-SIZE

new
50 gram

METI-DERM Aerosol

smaller, portable container
topical "Meti" steroid relief in a pocket-size dispenser that patients can carry with them

savings to patients
the advantages of topical "Meti" steroid therapy at a price comparable to many nonsteroid preparations

least wasteful
supplies sufficient medication for average short-term therapy at lower initial cost

quick relief
for poison ivy dermatitis, summer exacerbations of skin allergies

Schering

METI-DERM Aerosol—
50 Gm. container—16.6 mg. prednisolone.
150 Gm. container—50 mg. prednisolone.

METI-DERM,® brand of prednisolone topical.
Meti,® brand of corticosteroids.

METI-DERM with Neomycin Aerosol—
50 Gm. container—16.6 prednisolone and 16.6 mg. neomycin sulfate.
150 Gm. container—50 mg. prednisolone and 50 mg. neomycin sulfate.

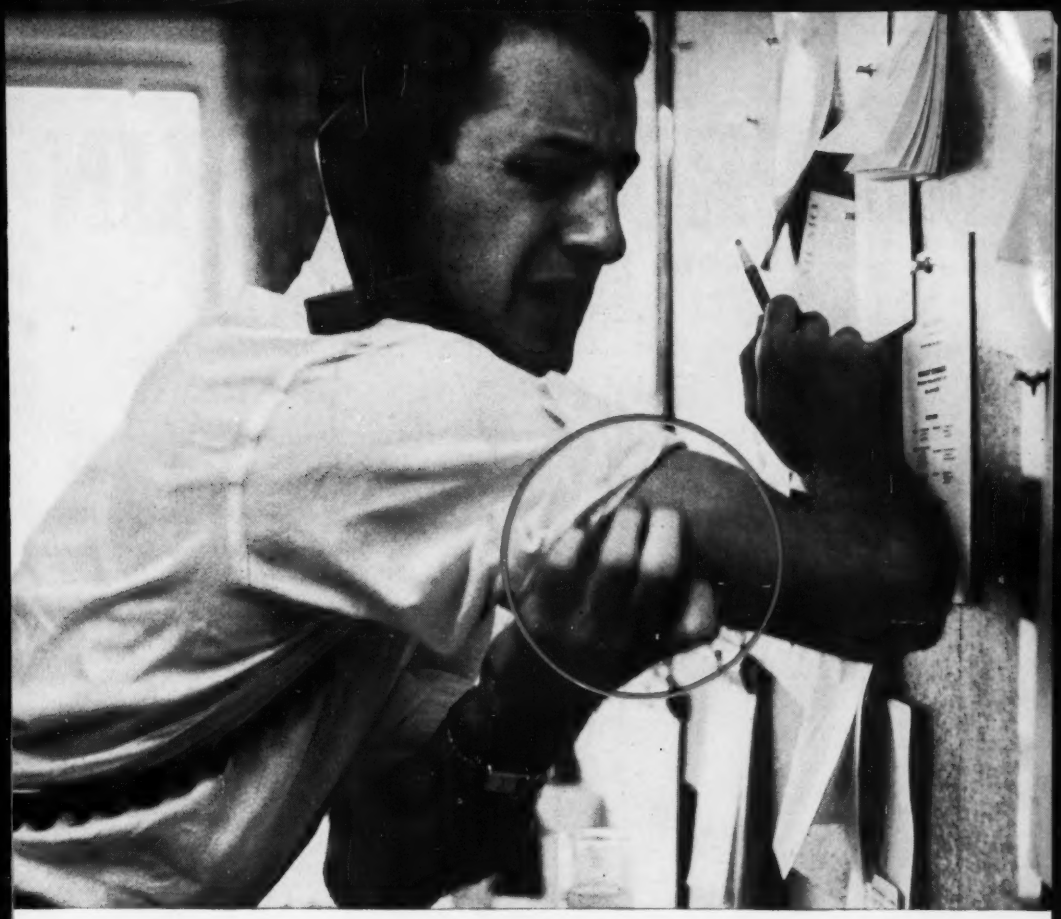
SCHERING CORPORATION · BLOOMFIELD, NEW JERSEY 5-165

The improved, new local anesthetic. What's the new, highly efficient local anesthetic for minor surgical procedures? Many physicians say it's Gebauer's new Fluro-Ethyl. An actual report: "I have used your mixture of 25% Ethyl Chloride and 75% "Freon" for skin planing and I find it most efficient for my purposes. Freezing is fast, each container lasts a long time, results are highly satisfactory".

Equally useful as a local anesthetic for incision of furuncles, electrocautery to small cutaneous tags, flat warts, nevi, and alleviation of needle pain in hypodermic injection. Non-flammable, requires no blower. Compare Fluro-Ethyl with the product you have been using. Gebauer Chemical Company, 9410 St. Catherine Avenue, Cleveland 4, Ohio.

① Gebauer's Ethyl Chloride in new Dispenseal amber glass. ② Metal tube for doctor's emergency kit. ③ Fluro-Ethyl in the aerosol container.

FLURO-ETHYL
GEBAUER
CHEMICAL COMPANY



Skin deep or deeper?

Certain skin disorders are due primarily to "nerves", others are often aggravated by anxiety, tension, and fear.[1]

'Miltown' therapy, 400 mg. t.i.d., relaxes the mind and allays somatic symptoms of anxiety and tension. It was used with encouraging results in a series of 164 patients with inflammatory skin conditions, including atopic, eczematoid and neurodermatitis, lichen planus, psoriasis, and anogenital pruritus.[2]

'Miltown' has been found "an effective addition to conventional dermatological therapy."[3] Results were achieved "without impairment of physical activity or mental alertness."[3]

References: 1. *Cahn, M. M.: The use of tranquilizing drugs in dermatology. J. Albert Einstein M. Center* **4**:*161, Sept. 1956.*
2. *LeVan, P. and Wright, E. T.: Use of tranquilizers in diseases of the skin – A preliminary report. California Med.* **85**:*87, Aug. 1956.*
3. *Sokoloff, O. J.: Meprobamate (Miltown) as adjunct in treatment of anogenital pruritus. A.M.A. Arch. Dermat. & Syph.* **74**:*393, Oct. 1956.*

Miltown®

meprobamate (Wallace)

WALLACE LABORATORIES, *New Brunswick, N. J.*

TO PROTECT SKIN

AGAINST A WIDE RANGE OF IRRITANTS

- *in industry*
- *in the home*

Silicote provides an important advance in protecting skin from dry and aqueous irritants—prophylactically to prevent skin maceration, and therapeutically to exclude water, soap, and other substances from dermatoses that may be aggravated by them.

Clinical tests show that Silicote provides excellent protection against soap and water and soluble cutting oils.[1]

The protective property of Silicote is purely mechanical. Protective efficiency is necessarily determined by the nature and frequency of exposure. Frequency of application should be adjusted to provide adequate protection with minimum dosage.

SUGGESTED DOSAGE: Cleanse area thoroughly with soap and water. Apply thin film as required and rub in well. If skin is exposed constantly to irritant, apply every 2-4 hours, or as needed to provide protection. It is not necessary to remove original coat before applying subsequent coats. Any objectionable greasiness may be removed by wiping with a dry cloth, or washing gently with soap and water.

CONTRAINDICATIONS: Do not use on weeping or infected areas.

In Housewife's Eczema
Industrial Dermatoses
Chapping—Chafing
Intertrigo
Diaper Rash
Chronic Dermatoses
Aggravated by Soap and Water

SILICOTE CONTAINS
30% dimethicone (silicone) in a specially prepared petrolatum base. Contains no water-soluble ingredients.

Send for samples and literature

1. Shaw, J. M., and Crowe, F. W.: Skin Protective Ointments. Arch. Dermat. & Syph. 71: 379, 1955.

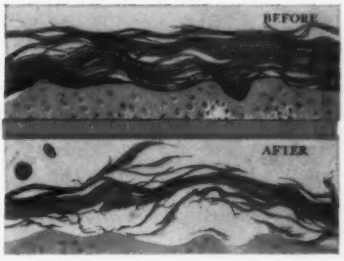
SILICOTE
SILICONE OINTMENT

ARNAR-STONE LABORATORIES, INC. MT. PROSPECT, ILLINOIS

In Canada: Brent Laboratories, Ltd., Toronto

New freedom from embarrassment and distress of psoriasis!

Alphosyl T.M. LOTION



DISAGGREGATES PSORIATIC SCALE

In vitro studies show that the keratin-dispersing action of allantoin is exceptionally effective in disaggregating psoriatic scale.[1,2] It apparently acts on an abnormal cement substance between cornified cells.[2,3] Coal tar, too, helps break up the horny layer.[2] Together, these agents provide rapid clearing of psoriatic lesions as well as the underlying inflammation and erythema.

ALPHOSYL Lotion, used by many physicians both in routine practice and in carefully controlled studies, proved highly successful.[2,4-7] The lotion permits complete avoidance of the potential hazards of certain other methods of treatment, such as superficial x-ray, heavy metals and corticosteroids.[7]

Advantages: • Treatment-fastness not observed • Cosmetic qualities permit free application to the scalp • Well tolerated • May be freely used on tender areas

FORMULA: Allantoin 2% and special coal tar extract 5% in a greaseless, stainless, vanishing lotion base.

SUPPLIED: Bottles of 8 fl. oz.

APPLICATION: For maximum therapeutic results rub thoroughly into lesions 2 to 4 times daily. For maintenance apply once or twice a week.

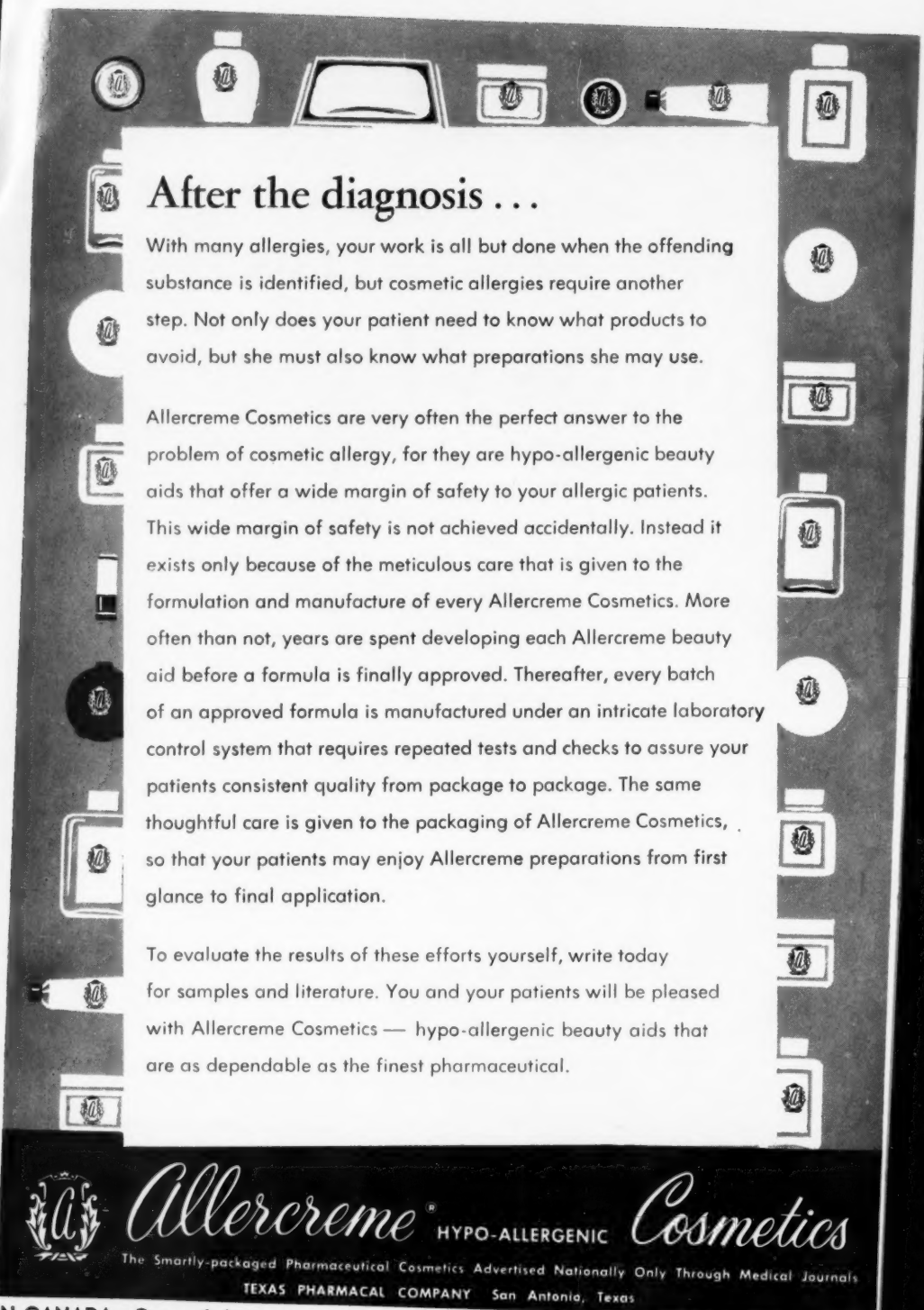
REFERENCES: 1. Flesch, P.: Proceedings Scientific Session. Toilet Goods Assoc. June, 1958. 2. Samitz, M. H.: Ann. New York Acad. Sc. 73:1020, 1958. 3. Flesch, P., and Jackson Esoda, E. C.: Ann. New York Acad. Sc. 73:989, 1958. 4. Bleiberg, J., and Saltzman, J. A.: Clin. Med. 5:485, 1958. 5. Bleiberg, J.: Ann. New York Acad. Sc.: 73:1028, 1958. 6. Clyman, S. G.: Ann. New York Acad. Sc. 73:1032, 1958. 7. Welsh, A. L., and Ede, M.: Ohio M. J.: to be published.

For psoriasis with acute inflammation

Alphosyl-HC T.M.

Alphosyl with 0.2% hydrocortisone
Supplied in bottles of 4 fl. oz.

R&C REED & CARNRICK
Jersey City 6, New Jersey



After the diagnosis . . .

With many allergies, your work is all but done when the offending substance is identified, but cosmetic allergies require another step. Not only does your patient need to know what products to avoid, but she must also know what preparations she may use.

Allercreme Cosmetics are very often the perfect answer to the problem of cosmetic allergy, for they are hypo-allergenic beauty aids that offer a wide margin of safety to your allergic patients. This wide margin of safety is not achieved accidentally. Instead it exists only because of the meticulous care that is given to the formulation and manufacture of every Allercreme Cosmetics. More often than not, years are spent developing each Allercreme beauty aid before a formula is finally approved. Thereafter, every batch of an approved formula is manufactured under an intricate laboratory control system that requires repeated tests and checks to assure your patients consistent quality from package to package. The same thoughtful care is given to the packaging of Allercreme Cosmetics, so that your patients may enjoy Allercreme preparations from first glance to final application.

To evaluate the results of these efforts yourself, write today for samples and literature. You and your patients will be pleased with Allercreme Cosmetics — hypo-allergenic beauty aids that are as dependable as the finest pharmaceutical.

Allercreme® HYPO-ALLERGENIC Cosmetics

The Smartly-packaged Pharmaceutical Cosmetics Advertised Nationally Only Through Medical Journals

TEXAS PHARMACAL COMPANY San Antonio, Texas

IN CANADA—Omega Laboratories, Ltd., Montreal and Toronto
IN CUBA—Laboratories Amedin, S. A., Habana
IN VENEZUELA—Salus, C. A., Caracas

unexcelled

potentiation • efficacy • toleration

in broad-spectrum antibiotic therapy

COSA-TERRAMYCIN®
oxytetracycline with glucosamine

capsules 125 mg. 250 mg. | *oral suspension* peach flavored, 125 mg. per teaspoonful (5 cc.), 2 oz. bottle | *pediatric drops* peach flavored, 100 mg. per cc. (5 mg. per drop), 10 cc. bottle (with calibrated dropper)

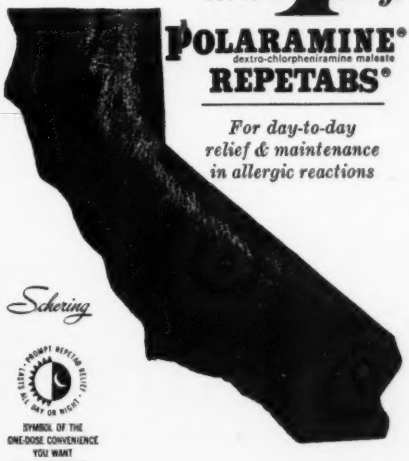
Pfizer *Science for the world's well-being*
PFIZER LABORATORIES
Division, Chas. Pfizer & Co., Inc.
Brooklyn 6, N. Y.

wherever the 4 winds blow

new 4 mg.

POLARAMINE®
dextro-chlorpheniramine maleate
REPETABS®

For day-to-day relief & maintenance in allergic reactions



Schering

PROMPT REPETAB RELIEF · LASTS ALL DAY OR NIGHT

SYMBOL OF THE ONE-DOSE CONVENIENCE YOU WANT FOR YOUR PATIENT

SCHERING CORPORATION • BLOOMFIELD, N. J. EN1486-9

AN *Ethix* FORMULA

UNSCENTED

SHAMPOO

Myristic and lauric acids saponified with polyamine alkali to a low pH(8), with neutralized polycarboxylic acid, enriched with lanolin esters, given extraordinary solvency with propylene glycol.

Vegetable or mineral tars may be added in desired percentage.

Removes ointments and medications gently but thoroughly.

High foaming, extremely economical in use.

Tolerated by scalps which shed epithelium from overstrong detergents.

RETAIL PRICE $1.50 BOTTLE 6 OZ.

ETHIX CORPORATION
P. O. Box 115, Inwood 96, L. I., N. Y.
Send 1 oz. sample bottles of ETHIX FORMULA Shampoo to:
.....M.D.
.....
.....

When your patient suffers from histamine-induced skin reaction

Whether caused by drugs, dander, or detergents, most histamine-induced skin reactions (such as the sulfonamide reaction shown above) respond rapidly to 'Teldrin' *Spansule* capsule therapy.

Just one capsule in the morning, another at night, provides 24-hour antihistamine effect. And because of the prolonged, even release of 'Teldrin' medication, side effects are minimal.

Teldrin® Spansule®

brand of chlorprophenpyridamine

brand of sustained release capsules

Smith Kline & French Laboratories, Philadelphia

WHETHER WET

OR WHETHER DRY

SUMMER DERMATOSES

such as poison ivy, sunburn and prickly heat promptly respond to soothing

AVEENO® Colloid Baths

if it's wet...

℞ **AVEENO Colloidal Oatmeal**

reduces inflammation... relieves pruritus... mildly drying for wet dermatoses

AVEENO Colloidal Oatmeal is available in 18 oz. and 4 lb. boxes.

if it's dry...

℞ **AVEENO "OILATED"**

(soothing colloidal oatmeal plus *35% emollient oils)*

lubricates the skin... softens dry, crusting lesions

AVEENO® "OILATED" colloidal oatmeal is available in 10 oz. cans.

AVEENO CORPORATION 250 West 57th Street New York 19, N. Y.

Pioneers in Ethically Promoted Colloid Baths

'B. W. & CO.'® ANTIBIOTIC LOTIONS FOR TOPICAL BACTERIAL INFECTIONS

Antibiotics

- Of proven effectiveness
- That rarely sensitize
- To which resistance or cross-resistance rarely develops clinically
- That are seldom used systemically

NEW

BACTERICIDAL ANTI-INFLAMMATORY

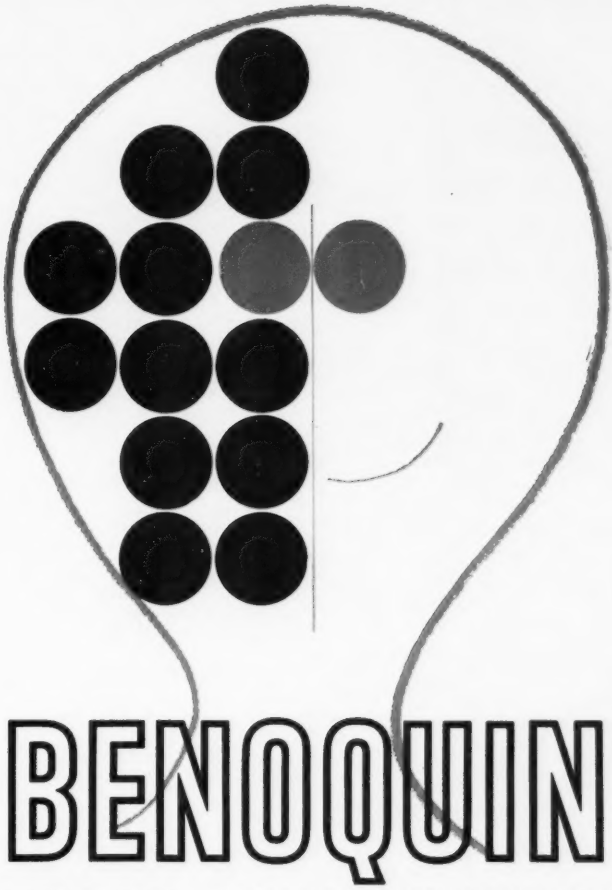
Each cc. contains:
'Aerosporin'®
brand Polymyxin B Sulfate
10,000 Units
Neomycin Sulfate...5 mg.
Hydrocortisone...(1%)10 mg.
in a special
water-miscible lotion
base. Plastic squeeze
bottles of 10 cc.

BACTERICIDAL

Each cc. contains:
'Aerosporin'®
brand Polymyxin B Sulfate
10,000 Units
Neomycin Sulfate...5 mg.
in a special
water-miscible lotion
base. Plastic squeeze
bottles of 20 cc.

The assurance of proven formulas—
"Cosmetically acceptable"
to the patient

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, New York



BENOQUIN®

REVERSES HYPERPIGMENTATION

BENOQUIN, brand of monobenzone, Elder, inhibits the formation of pigment by the melanin producing cells of the skin. Applied topically to areas of hyperpigmentation due to excessive melanin production it usually results in depigmentation and disappearance of the disfiguring patches.

Available as BENOQUIN Ointment, 20%, in 1¼ oz. tubes and 1 lb. jars; and as BENOQUIN Lotion, 5%, in 4 oz. bottles, for the treatment of such hyperpigmentation states as: ■ Generalized lentigines ■ Severe freckling ■ Melasma of Addison's disease or pregnancy ■ Berlock dermatitis ■ Following inflammation of the skin

ELDER

Write for literature and patient instruction forms PAUL B. ELDER COMPANY, Bryan, Ohio

ACCUMULATING EVIDENCE shows the

CLINICAL STUDY OF CADMIUM SULFIDE SHAMPOO

Canad. M. A. J. *79*:917 (Dec. 1) 1958

"In treatment of seborrhoea of the scalp with cadmium sulfide 1% (Capsebon), a good result was obtained in 71% of the 127 cases, a fair result . . . in 15%, and no result in 14%. The preparation is an excellent shampoo. Its use does not bring about 'rebound' oiliness. No toxic side effects were seen."

J. H. HARVEY, M.D., and L. P. EREAUX, M.D.

PRELIMINARY AND SHORT REPORT
CADMIUM SULFIDE SHAMPOO IN SEBORRHEA CAPITIS

J. Invest. Dermat. *29*:159 (Sept.) 1957

"Of eighty-four patients treated for seborrheic problems in the scalp with . . . cadmium sulfide shampoo . . . seventy-nine [94%] obtained good to excellent results."

W. L. KIRBY, M.D.

New Beneficial Agents in the Treatment of Acne Vulgaris and Seborrheic Dermatitis

Postgrad. Med. *24*:439 (Oct.) 1958

" . . . this preparation does appear to be one of the better antiseborrheic agents. The effectiveness and cosmetic acceptability of this preparation would appear to warrant its further use."

D. G. STOUGH, M.D.; ROBERT LEWIS, M.D.; B. L. FARMER, M.D.; L. S. OSMENT, M.D., and R. O. NOOJIN, M.D.

Cadmium Shampoo Treatment Of Seborrheic Dermatitis

Texas J. Med. *53*:640 (Aug.) 1957

" . . . an extremely useful agent in control of chronic or recurrent seborrhea of the scalp . . . an important contribution . . . "

J. FRED MULLINS, M.D., and JAMES R. BARNETT, M.D.

effectiveness of this therapeutic shampoo

BEFORE

AFTER

THESE STATEMENTS REFLECT THE GROWING RECOGNITION OF CAPSEBON'S

- effectiveness
- high degree of safety
- cosmetic acceptability

Capsebon is easy to apply—easy as an ordinary shampoo, and just as quick.

Available in 4-oz. bottle, on prescription only.

Additional references available from Professional Service Department on request.

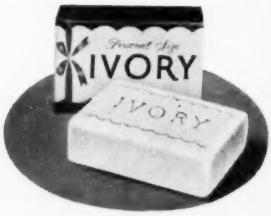
Capsebon™

1% cadmium sulfide suspension

PITMAN-MOORE COMPANY
DIVISION OF ALLIED LABORATORIES, INC.
INDIANAPOLIS 6, INDIANA

Picture of Ivory Soap's 234th... and most crucial ...test

Nothing is more important to Ivory than unofficial "test" #234—the mild, daily care this white, pure soap gives babies and adults in homes everywhere. But first come 233 laboratory and scientific tests to make sure not a single cake reaches step #234 unless it meets the highest standards of purity and mildness. This is the kind of supervision that makes Ivory gentle enough for even delicate baby skin. You can advise Procter & Gamble's Ivory Soap confidently.



99 44/100% pure® ... it floats

For acne and pimples with extensive flush areas

Acne Cort-Dome™

Hydrocortisone with sulfur, bithionol, resorcinol monacetate, in aluminum acetate vehicle pH 5.0

CREME or LOTION

DOME

antiinflammatory/keratolytic

INCORPORATED IN EXCLUSIVE ACID MANTLE VEHICLE

Within a short period of time suppresses the epidermatitis of acne, reduces erythema, allays inflammation, soothes acute exacerbations and produces enough peeling action to gently open the papules and pustules. Restores and maintains normal acidity of the skin.

SIG: Apply morning and night to skin after washing and at night to scalp.

SUPPLY: Creme in 1 oz. tubes. Lotion in 1 oz. squeeze bottles. Samples and literature on request.

DOME CHEMICALS INC.

NEW YORK 23 LOS ANGELES 46

IN CANADA: 2765 BATES RD., MONTREAL, P. Q.

A TRUSTED NAME IN DERMATOLOGICALS

in "burns, ulcers and sloughing wounds... successful" *

*In "burns, ulcers and sloughing wounds... a decrease in purulent material, cleaner granulation tissue and an increased rate of epithelization...[PANAFIL] proved to be a successful chemical débriding agent...no effect on viable tissue, and the complications were relatively few in number and were never serious." —Katz, R. I.; Reese, J. W., and Byrne, J. J.: Am. J. Surg. 95:102, 1958.

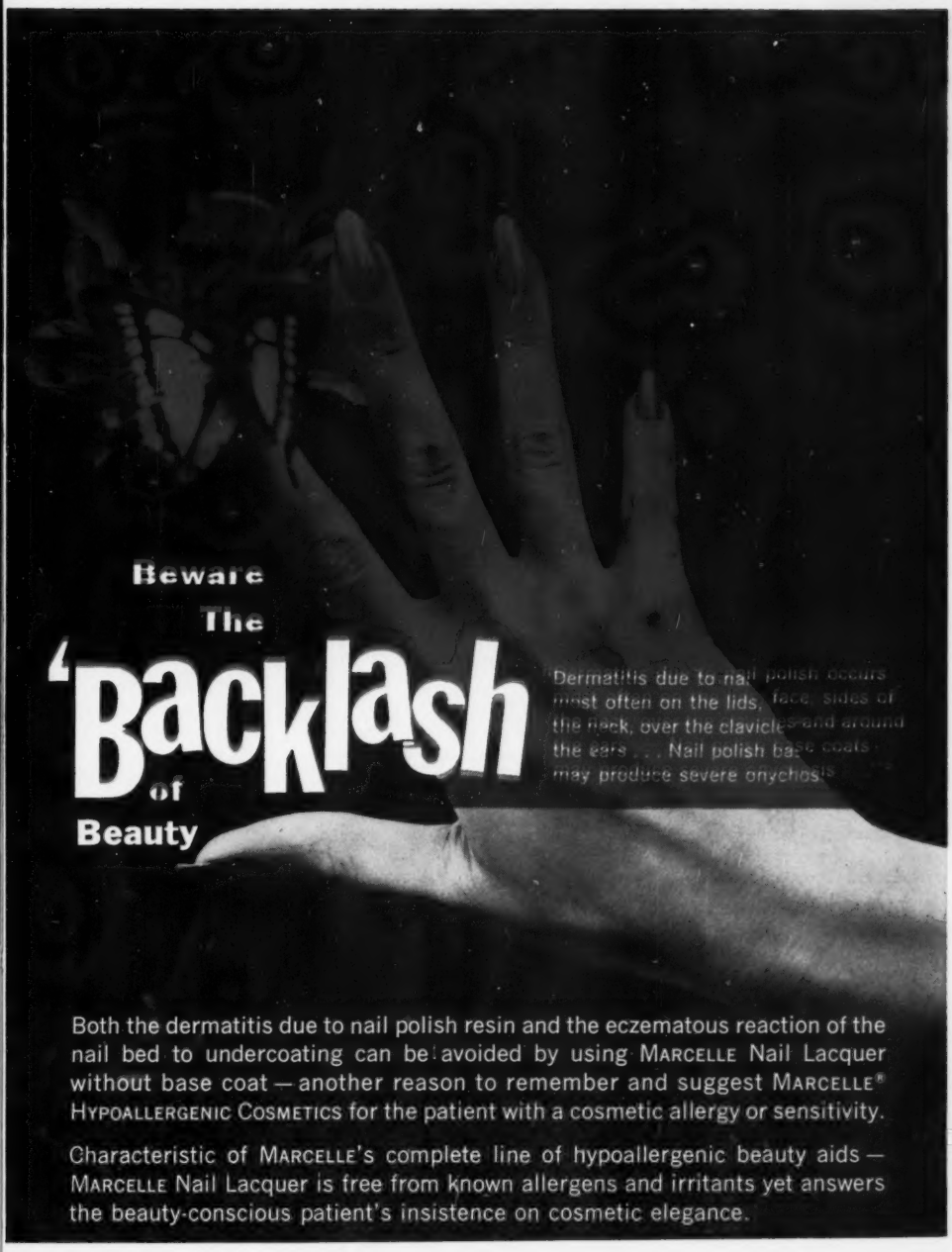
Rystan
Mount Vernon, N.Y.

panafil® topical enzyme therapy

- effective wound cleansing and healing
- well tolerated and convenient for outpatient use
- economical for hospital and patient

PANAFIL ointment (papain—urea—water-soluble chlorophyll derivatives) • For complete information see your Physicians' Desk Reference

32459


Beware
The
'Backlash
of
Beauty
Dermatitis due to nail polish occurs most often on the lids, face, sides of the neck, over the clavicles and around the ears . . . Nail polish base coats may produce severe onychosis*

Both the dermatitis due to nail polish resin and the eczematous reaction of the nail bed to undercoating can be avoided by using MARCELLE Nail Lacquer without base coat — another reason to remember and suggest MARCELLE® HYPOALLERGENIC COSMETICS for the patient with a cosmetic allergy or sensitivity.

Characteristic of MARCELLE's complete line of hypoallergenic beauty aids — MARCELLE Nail Lacquer is free from known allergens and irritants yet answers the beauty-conscious patient's insistence on cosmetic elegance.

Marcelle COSMETICS

Borden's PHARMACEUTICAL DIVISION
350 Madison Avenue, New York 17

Available in Canada through Prof. Sales Corp., Montreal

*Andrews, G. C.: Diseases of the Skin, ed. 4, Philadelphia, Saunders, 1954, pp. 117, 118

BUCKY

PIONEER NAME IN X-RAY . . .

Has an Ideal unit for the Dermatologist . . .

COMBINATION THERAPY APPARATUS

SPECIAL RAIL-MOUNTED FEATURES: Permits positioning of tube head as low as floor. Also, portion of patient's body facing the wall, can be positioned without turning patient.

MODEL G-3S
RAIL-MOUNTED

SUPERFICIAL, CONTACT & GRENZ RAY THERAPY

from a half value layer as high as 4.0 (mm.al) at 400r units per minute to a half value layer of 8 microns.

for the price of one!

MODEL G-3w
Wall-mounted unit; tube holder arm and control unit installed according to your specifications. Takes up no floor space.

SAFE: provides positive radiation control. The protective automatic filter slide circuit affords the ultimate in patient protection. No radiation can be produced with this apparatus above 15 KV, unless added filtration is provided.

POSITIONING FEATURES: Counterbalanced tube holder arm permits the positioning of the tube port in any position, without loosening or tightening any locks. No external wires to tube head. Continuous rotation of tube head.

ADAPTABLE: No special wiring or current required since the units operate from the standard house current of 110 volts on 20 amp fuse.

WHOLE BODY RADIATION: Due to increased output whole body radiation is now possible in single exposures with practical outputs.

EFFICIENT: Approximately 80% of the depth dosage is in the first 4 millimeters of the skin, due to the employment of a BERYLIUM window tube.

VERSATILE: Wide range of field sizes for X-ray or Grenz ray therapy in a single exposure can now be obtained due to the increased output.

CONTINUOUS FLEXIBLE DEPTH CONTROL: is assured by stepless KV control.

DURABLE: Long tube life guaranteed by overrating of tube voltage.

MODEL G-3 MOBILE
Completely mobile, no installation needed.

Sales and factory-controlled Service in all major Cities and Countries

The International Medical Research Corp.

60 East 42nd S
New York, N.

MIR

Write for comprehensive literature on this and other time-teste
***BUCKY** Straight X-Ray and Grenz Ray Therapy machines*

Please send complete information on Model(s) # _____

Name: _____

Address: _____

City: _____

ORIGINATORS of the COMBINATION THERAPY UNIT. PIONEERS of the GRENZ RAY THERAPY APPARAT

In eczematous dermatitis with secondary infection CREME AND LOTION pH 5.0

COR-TAR-QUIN™

DOME

HYDROCORTISONE • STAINLESS TAR • DIIODOHYDROXYQUINOLINE
IN ALUMINUM ACETATE VEHICLE

COR-TAR-QUIN is especially effective in those dermatoses where an inflammatory reaction is accompanied by increased scaling, lichenification, and secondary infection.

Combined hydrocortisone-coal tar therapy produces an enhanced antipruritic, anti-inflammatory response and diiodohydroxyquinoline is fungicidal as well as bactericidal. The Acid Mantle creme base of COR-TAR-QUIN helps restore and maintain normal pH of the skin. Relief is prompt and lasting.

Sig: Apply b.i.d. ½ oz., 2 oz., and 4 oz. tubes with either 0.5% or 1.0% hydrocortisone

also available without the stainless tar, as CORT-QUIN™ CREME pH 4.5

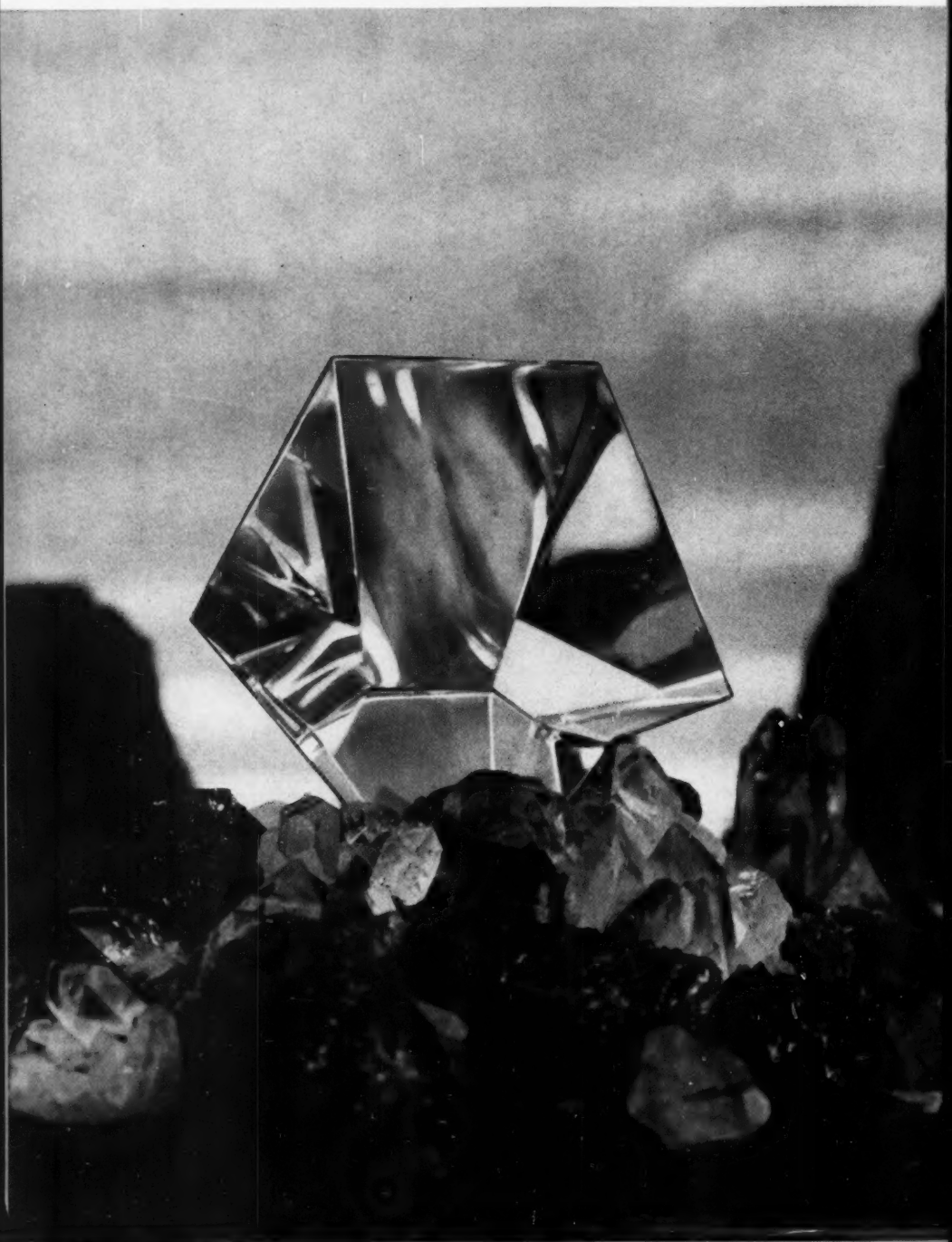
INCORPORATED IN EXCLUSIVE ACID MANTLE VEHICLE

A MOST TRUSTED NAME IN DERMATOLOGICALS

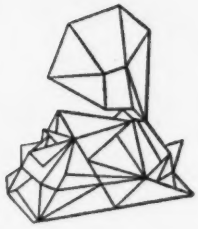
DOME CHEMICALS INC.

125 West End Avenue, New York 23, N. Y.
665 N. Robertson Blvd., Los Angeles 46, Cal.
2765 Bates Road, Montreal, Canada

PURE ANTIHISTAMINE ACTION A PHARMACOLOGIC FACT BECAUSE DĪSOMER SHEDS THE MOLECULAR DROSS



NEW...IN THE TREATMENT OF ALLERGIC DISORDERS



- *"...high therapeutic index"*[1]
- *unsurpassed clinical efficacy*
- *highly effective in exceptionally small doses*
- *side effects reduced to minimal level*

Disomer....a scientific contribution in the pharmacology of antihistamines!

Incorporating the newest knowledge of structure-function relationships, DISOMER comes close to the therapeutic ideal of pure antihistamine activity. DISOMER represents the *d*-isomer of racemic brompheniramine maleate. In shedding the *l*-isomer a high point in clinical effectiveness is achieved while side effects are reduced to a minimal level.

Therapeutic results have been noteworthy with 88% effectiveness reported.[2] Equally noteworthy is the low incidence of clinically significant adverse reactions. Indeed, the sole side effect reported was occasional, mild drowsiness in only 5% to 6% of patients.

With DISOMER your allergic patient remains your alert patient while enjoying unsurpassed freedom from allergic symptoms. Ready now for your prescription—DISOMER is available in a variety of dosage forms to fit your patients' individual requirements.

Availability:

DISOMER CHRONOTAB*	6 mg.
DISOMER CHRONOTAB*	4 mg.
DISOMER Tablets	2 mg.
DISOMER Syrup	2 mg. per 5 cc.

Usual dosage:

6 mg. CHRONOTAB	b.i.d.
4 mg. CHRONOTAB	t.i.d.
2 mg. Tablet	q.i.d.
Syrup 1 teaspoonful	q.i.d.

**Chronotab* is White's repeat-action tablet.

References: (1) Gould, A. H. and Long, D. L.: Clinical Pharmacology and Therapeutic Use of Dexbrompheniramine Maleate (Disomer), a new Histamine Antagonist (submitted for publication). (2) Medical Department, White Laboratories, Inc.

WHITE LABORATORIES, INC.
Kenilworth, New Jersey

DISOMER

DEXBROMPHENIRAMINE MALEATE

...sheds the molecular dross

In Acne

TUCKS®

soft cotton flannel pads saturated with witch hazel (50%) and glycerine (10%), pH about 4.6

answers a dermatologic and an emotional need

Cleansing, solvent, mildly astringent TUCKS provides a new and valuable therapeutic aid for the treatment of acne.

At home in their handy jars, or *at school* in the moisture-tight plastic envelope provided, soothing Tucks pads promote the thorough skin care indispensable to the successful treatment of acne.

Always ready for use, TUCKS encourages cleanliness when used as finger shields for expressing comedones.

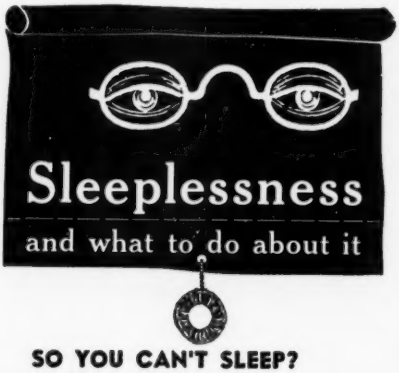
fuller PHARMACEUTICAL COMPANY
Minneapolis 16, Minn.

For a generous office supply of TUCKS —just fill in and return this card.

Name_____

Address_____

City_____ Zone____ State_____

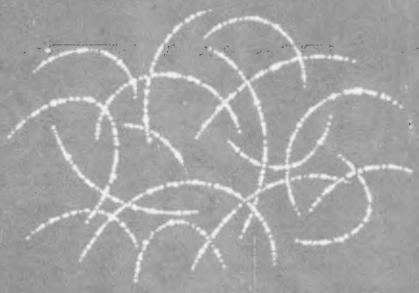


SO YOU CAN'T SLEEP?
by P. H. Fluck
8 pages, 15 cents

SLEEPLESSNESS AND WHAT TO DO ABOUT IT by Donald A. Laird, Ph.D.
8 pages, 15 cents

ROADS TO RELAXATION
by Joseph L. Fetterman, M.D.
4 pages, 10 cents

AMERICAN MEDICAL ASSOCIATION
535 N. Dearborn St., Chicago 10, Illinois



Used in every type of practice and clinical specialty today, EQUANIL® (meprobamate, Wyeth) has proved that anxiety and tension *can* be controlled to smooth the course of diagnosis, treatment, and convalescence. Anxiety is a fact of life. Anxiety is a fact of illness.

Wyeth
®
Philadelphia 1, Pa.

FRIGIDERM®

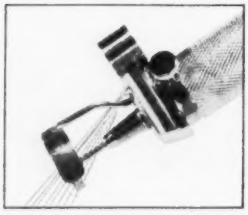
(100% dichloro-tetrafluoro-ethane...contains no ethyl-chloride)

SKIN REFRIGERANT–ANESTHETIC

*Widely Accepted for Local Anesthesia in Surgical Planing of the Skin**

JET-SPRAY PLANER

This hand-tooled, precision-built instrument with diamond fraises is available for most standard planing units. In ordering, please specify make of planing unit. Full information on request.



FRIGIDERM has been researched and developed to meet th expressed need of physicians for a well tolerated skin refrig erant-anesthetic...non-explosive, non-inflammable...havin no general anesthetic properties.

Today, **FRIGIDERM** is one of the preferred products of it kind among Dermatologists everywhere.

FRIGIDERM quickly produces local anesthesia for surgica planing in the treatment of scarring due to acne, chickenpox smallpox and trauma...multiple senile keratoses...fin wrinkling...traumatic tattoos.

Also for incision of furuncles, electrocautery to smal cutaneous tags, flat warts, or for alleviation of needle pai during hypodermic injection.

This freezing agent can be delivered from the spray-to container shown above by easy finger pressure.

Now in the improved 8 oz. container — $2.00

Fully guaranteed for satisfactory performance
Available at your surgical supply dealer

*A.M.A. Archives of Dermatology, April 1955
Ref.: Wilson, J. W.; Lukart II, R.; Ayres III, S.. Reprints available*

® REGISTERED TRADE MARK

W. T. BRACHVOGEL

1723 WEST SEVENTH STREET • DUNKIRK 4-9273 • LOS ANGELES 17, CALIFORNI

So many of the patients who open your door exhibit the common, non-inflammatory skin conditions in which steroids may be of little or no value.

SEBORRHEIC AFFECTIONS, especially of the scalp, such as "cradle cap" and dandruff

FUNGOUS INFECTIONS, including "athlete's foot," tinea capitis, etc.

SUBACUTE AND CHRONIC DERMATITIS where scaling and lichenification may be a problem

ECZEMATOUS ERUPTIONS following acute dermatoses of various etiologies

These are the candidates for the gentle keratolytic-bacteriostatic action of 'Pragmatar'.

PRAGMATAR®

an outstanding tar-sulfur-salicylic acid ointment

SKF Smith Kline & French Laboratories

ALCOHOLISM

an important problem in today's living!

The following articles from TODAY'S HEALTH are now available in one pamphlet for 50 cents . . .

ALCOHOLICS ANONYMOUS. Written from the standpoint of a member, the basic treatment procedures are described and the psychological problems confronting the alcoholic are discussed.

ALCOHOL AND CIRRHOSIS OF THE LIVER. Relationship between alcohol, diet and cirrhosis. Increasing stress on nutritional differences. by Russell S. Boles

HOW TO HELP A PROBLEM DRINKER. Understanding the alcoholic's capabilities, the necessity of help, causes of his condition. by Edward A. Strecker and Francis T. Chambers, Jr.

THE TREATMENT OF ALCOHOLISM. Tracing the steps from convincing the alcoholic that he is sick through treatment and cure. by Lewis Inman Sharp

CONDITIONED REFLEX TREATMENT OF CHRONIC ALCOHOLISM. its place among methods of treatment today, its development and correlation with personality factors. by Walter L. Voegtlin

INSTITUTIONAL FACILITIES FOR THE TREATMENT OF ALCOHOLISM. Comparative differences, in drinking, with the last century, new establishments and methods of treatment, lack of trained personnel. by E. H. L. Corwin

other pamphlets available . . .

ALCOHOLISM IS A DISEASE. A discussion by the Chairman of the A.M.A.'s Committee on Alcoholism. by Marvin A. Block, M.D., 8 pages, 15 cents

I AM THE WIDOW OF AN ALCOHOLIC. Three articles combined. by Virginia Conroy, 16 pages, 20 cents

HOW EXPERTS MEASURE DRUNKENNESS. A partial transcript of an actual courtroom case. by H. A. Heise, 8 pages, 15 cents

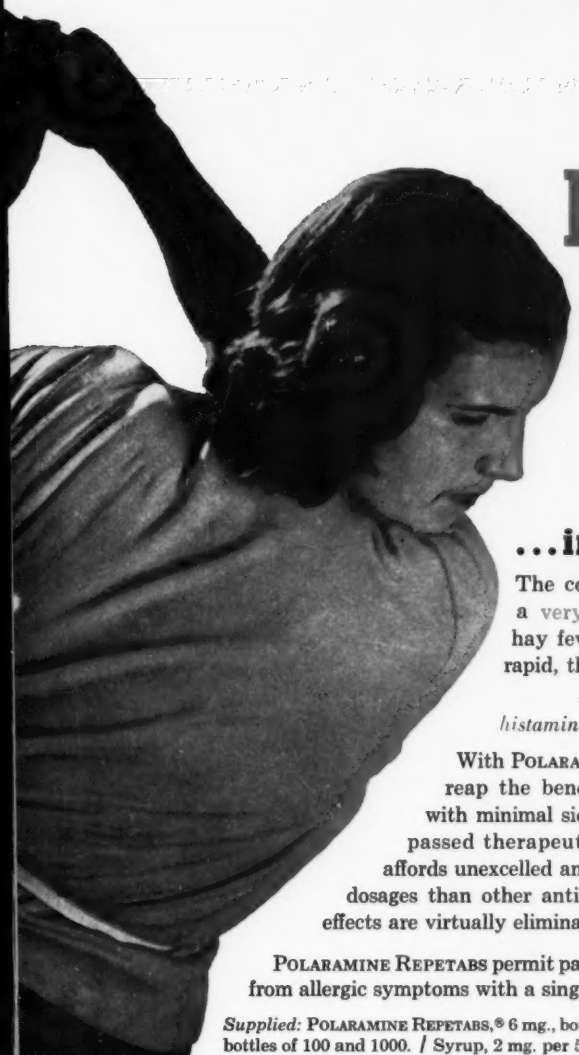
BARBITURATES, BOOZE AND OBITUARIES. A discussion of the dangers of mixing alcohol and barbiturates. by Donald A. Dukelow, 4 pages, 10 cents

TWELVE STEPS FOR ALCOHOLICS. A frank discussion of the meaning of an alcoholic behavior. by Richard Lake, 6 pages, 10 cents

address requests to . . .

ORDER DEPARTMENT

AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS



DANGER IN THE ROUGH

...inviting pollenosis

The control of allergic symptoms is a very important problem for your hay fever patient. You can prescribe rapid, thorough relief with POLARAMINE

—close approach to a perfect antihistamine.

With POLARAMINE your hay fever patient can reap the benefits of antihistamine therapy with minimal side effects. Because of its unsurpassed therapeutic effectiveness, POLARAMINE affords unexcelled antihistaminic protection at lower dosages than other antihistamines...and annoying side effects are virtually eliminated.

POLARAMINE REPETABS permit patients daylong or nightlong relief from allergic symptoms with a single medication.

Supplied: POLARAMINE REPETABS,® 6 mg., bottles of 100 and 1000. / Tablets, 2 mg., bottles of 100 and 1000. / Syrup, 2 mg. per 5 cc., bottles of 16 oz.

SYMBOL OF THE ONE-DOSE CONVENIENCE YOU WANT FOR YOUR PATIENT

PROMPT REPETAB RELIEF · LASTS ALL DAY OR NIGHT ·

POLARAMINE* MALEATE

dextro-chlorpheniramine maleate

SCHERING CORPORATION · Bloomfield, New Jersey

*T.M. EN1478-9

Schering

Incorporated in exclusive ACID MANTLE vehicle

Quick Soothing Topical Response

IN INFLAMMATORY DERMATOSES

Cort-Dome™

Acid Mantle-Hydrocortisone

CREME AND LOTION—pH 4.6

ABATES INFLAMMATION AND RESTORES NORMAL SKIN ACIDITY

"Susceptibility to infection by bacteria is widely held to be due to the removal of the antibacterial 'acid mantle' of the skin and its displacement by an abnormal 'alkaline mantle'."—Fabricant, N. D.: A. M. A. Arch. Otolaryn. 65:11, 1957.

Supply—⅛%, 1% and 2% hydrocortisone in either Creme (⅛ oz., 1 oz., 2 oz., 4 oz. tubes and 1 lb. jars) or Lotion (½ oz., 1 oz., 2 oz., 4 oz. squeeze bottles and pt. bottles).

Samples and literature available on request.

Dome Chemicals Inc.

NEW YORK 23 • LOS ANGELES 46 • In Canada: 2765 Bates Road, Montreal

topical strategy...

ACHROMYCIN OINTMENT 3%

r infectious dermatoses. Unsurpassed broad-spec-m control of causative organisms and complicating xed invaders. Excellent local toleration; low sensitiz- potential. In ½ oz. and 1-oz. tubes.

ACHROMYCIN OINTMENT 3% WITH HYDROCORTISONE 2%

For inflammatory dermatoses. Classic corticoid suppression of erythema, swelling, weeping, pruritus... plus ACHROMYCIN control of pyogenic or subclinical secondary infection. In 5 Gm. tube.

ACHROMYCIN®

cycline Lederle

RLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, New York Lederle

New

LIQUIMAT

A new tinted lotion containing 5% precipitated sulfur for the local treatment of acne. Resorcin, calamine, phenol, menthol, camphor, betanapthol and coal tar solution may be added. To individualize your prescription further, the three shades may be interblended. In 3 ounce plastic bottles.

a fine, dependable, flexible line for the treatment of . . .

acne

SULFORCIN LOTION

contains 5% dispersible sulfur and 3% resorcinol monoacetate in a colloid-processed base of citrus pectin. Sulforcin Lotion dries rapidly, holding sulfur securely to the skin. Non-sticky, non-greasy, non-staining.

SULFORCIN CREAM

contains 5% dispersible sulfur and 3% resorcinol monoacetate in a water soluble vanishing cream type base. Lubricating and washable, Sulforcin Cream is especially suitable for application to large areas, and where dryness exists.

SULFORCIN BASES

a greaseless cream type make-up base supplied in 2* strengths and 3 shades which enable you to prescribe more individually for your patients' needs. Sulforcin Base helps conceal blemishes and is an excellent make-up foundation.

SEBA-NIL

Clinical studies prove conclusively that very oily skins respond more rapidly to acne therapy when cleansed with Seba-Nil rather than soap and water. Seba-Nil contains organic solvents and a mild, non-ionic detergent which make it more efficient than soap and water in preparing oily skin for medication.

**Also available: Plain Resorin-free Sulforcin Base, containing 2½% sulfur only.*

For detailed information and samples, write . . .

TEXAS PHARMACAL COMPANY

San Antonio, Texas

IN CANADA—Omega Laboratories, Ltd., Montreal and Toronto

three-way comparative study demonstrates "full-healing effect" of HYDRO-TAR™ in acute & chronic dermatoses

(Liquor Carbonis Detergens with Hydrocortisone, Almay)

A CASE IN POINT—ATOPIC DERMATITIS OF BOTH HANDS

1. Hydrocortisone alone suppresses inflammation. 2. Coal tar alone corrects eczematous manifestations. 3. Both agents combined in HYDRO-TAR speed complete early healing. Mutually supportive action produces the "full-healing" effect. Presence of hydrocortisone permits well-tolerated coal-tar therapy even during the acute phases of severe dermatoses.

Dosage: **Apply by gentle massage to affected areas 3 or 4 times a day; 0.5% for moderately severe dermatoses or maintenance – 1.0% for severe dermatoses.**

Supplied: **15 Gm. tubes in 0.5% and 1.0% strengths. Samples and literature sent on request.**

ALMAY Division of *Schieffelin & Co. / Since 1794*
Pharmaceutical Laboratories Division, New York 3, New York

Schieffelin 1794 Quality Integrity Service

A PHYSIOLOGIC WET DRESSING FOR SKIN DISORDERS

PROPHYLLIN®

POWDER FOR WET DRESSINGS

PROPHYLLIN combines sodium propionate, a constituent of the protective secretion of normal skin, with water-soluble chlorophyllin. The result is a **natural,** nontoxic wet dressing, soothing in the most acutely inflamed skin disorders. It can be used even around the eyes and genitalia—or as a mouthwash—without fear of irritating the mucous membranes.

PHYSIOLOGIC: contains no chemical irritants or sensitizing agents

NONASTRINGENT: will not block sweat ducts

MARKEDLY ANTIPRURITIC

MILDLY BACTERIOSTATIC AND FUNGISTATIC

COSMETICALLY ACCEPTABLE: no staining, no objectionable odor

SUPPLIED:
In cartons of 12 packets. (Each packet contains 2.3 gm. of powder, for preparation of 8 fluid ounces of solution containing 1% sodium propionate and 0.0025% water-soluble chlorophyllin.) Also in 4-ounce and 16-ounce jars.

Rystan company MOUNT VERNON, NEW YORK

31559

NEW

rich, creamy lather
with improved

LOWILA® CAKE

NEW . . . because Lowila* Cake has undergone a change. It now provides a rich, creamy, more abundant lather and has a smoother feel.

Lowila Cake cleans tender or dermatitic skin with virtually no irritation. It maintains the skin's normal acid lipid film and creates an environment favorable to therapy and healing.

*Contains sodium lauryl sulfoacetate in a corn dextrin base, acidified with lactic acid.

In bar form. Write for samples.

WESTWOOD PHARMACEUTICALS
BUFFALO 13, NEW YORK

Fostex®
treats their acne while they wash

degreases the skin helps remove blackheads dries and peels the skin

...and this is how it works

Fostex provides essential actions necessary in treating acne. It washes off excess oil. It unblocks pores by penetrating and softening blackheads. It dries and peels the skin, removing papule coverings, thus permitting drainage of sebaceous glands.

Fostex contains Sebulytic®,* a combination of surface-active wetting agents with remarkable antiseborrheic, keratolytic and antibacterial actions . . . enhanced by sulfur 2%, salicylic acid 2%, hexachlorophene 1%.

*sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate and sodium dioctyl sulfosuccinate.

Your patients will like Fostex because it is so simple to use. They simply wash acne skin 2 to 4 times a day with Fostex, instead of using soap.

FOSTEX CREAM

. . . in 4.5 oz. jars. For therapeutic washing in the initial phase of oily acne treatment.

FOSTEX CAKE

. . . in bar form. For therapeutic washing to keep the skin dry and free of blackheads during maintenance therapy. Also used in relatively less oily acne.

Write for samples.

WESTWOOD PHARMACEUTICALS • **Buffalo 13, New York**

A.M.A. ARCHIVES OF
DERMATOLOGY

Bowen's Disease and Its Relationship to Systemic Cancer

JAMES H. GRAHAM, M.D., and ELSON B. HELWIG, M.D., Washington, D. C.

Introduction

In this paper we shall report a previously unrecognized association of Bowen's disease of the skin with primary internal cancer.

Bowen,[1] in 1912, described two patients with atypical epithelial proliferation of the skin. Each patient had a chronic solitary lesion composed of lenticular papules resembling a noduloulcerative syphiloderm.

Darier,[2] in 1914, Bowen,[3] in 1915, and, more recently, Fraser[4] described multiple, nonelevated, scaly or crusted plaques as a variety of Bowen's disease. Histologically, these lesions were indistinguishable from those reported originally by Bowen.

Submitted for publication March 6, 1959.

From the Armed Forces Institute of Pathology.

This investigation was supported in part by a research grant, No. C-3799, from the National Cancer Institute, Public Health Service, Bethesda 14, Md.

The manuscript was awarded second prize by the Research Aid Committee of the American Dermatological Association, Inc. (Eighth Annual Essay Contest).

The authors wish to acknowledge the contributions of Mrs. Mardelle L. Reynolds, Mr. B. L. Parnell, and Mrs. Mote E. Dann of the Medical Statistics Section and M/Sgt. W. F. Engler, Photography Division, Armed Forces Institute of Pathology.

Earl D. Osborne Fellow in Dermal Pathology of the American Academy of Dermatology and Syphilology. Present position: Assistant Professor of Dermatology, Temple University Medical Center, Philadelphia (Dr. Graham). Chief, Department of Pathology, Armed Forces Institute of Pathology (Dr. Helwig).

Since Bowen's original description, many similar lesions have been recorded. Furthermore, the concept has been broadened by some investigators to include sites other than the skin, such as the oral cavity, anus, eye, genital organs, and genitourinary tract. We shall record our experience and observations of a large group of patients with Bowen's disease of the skin which meet the criteria originally described by Bowen[1] and later by Darier[2] and Fraser.[3]

Materials and Methods

This study was conducted at the Armed Forces Institute of Pathology and based on 35 patients with Bowen's disease of the skin who either came to autopsy or who were known to have died after surgical specimens were examined. Clinical and gross pathologic observations were supplemented by clinical records, surgical reports, death certificates, and autopsy protocols. All tissues were fixed in 10% formalin solution. Sections of the lesions of the skin and internal organs stained with hematoxylin and eosin were examined in all cases. Identical procedures were performed on surgical and autopsy material from controls consisting of 35 patients with senile keratosis and 35 with squamous-cell carcinoma of the skin. Additional controls were 139 patients with exfoliative dermatitis; autopsy material was available on 95 of these. For comparison in regard to the incidence of internal cancer, material was examined from patients with the following diseases: arsenical keratosis, erythroplasia of Queyrat, Paget's disease, extramammary Paget's disease, xeroderma pigmentosum, acanthosis nigricans, dermatomyositis, poikiloderma atrophicans vasculare, herpes zoster, Kaposi's sarcoma, and carcinoid.

Supplementary statistical data were obtained from follow-up of more than 100 living patients

TABLE 1.—*Age Distribution of Patients at Surgical Biopsy or Removal of Bowen's Lesions*

Age, Yr.	Patients, No.	%
38-39	1	3
40-49	3	9
50-59	10	28
60-69	13	37
70-79	7	20
80-87	1	3
Total	35	100

TABLE 2.—*Sites of Bowen's Lesions with Material Available for Microscopic Study*

Site	No.	%
Head		
Temple	5	
Nose	1	
Cheek	4	
Ear	9	
Forehead	1	
Preauricular	1	
	(21)	44
Neck	1	1
Trunk		
Abdomen	1	
Upper back	1	
Lower back	4	
	(6)	13
Extremities		
Arm	5	
Hand	7	
Thigh	1	
Leg	1	
	(14)	29
Pelvic area		
Buttocks	2	
Hip	2	
Groin	1	
Perineum	1	
	(6)	13
Total	48	100

with Bowen's disease of the skin and from a review of the literature.

Clinical Data and Gross Pathology

Race and Sex.—All of the 35 patients with Bowen's disease of the skin were Caucasians. Thirty-two were men, and three were women. The source of most of the material at the Armed Forces Institute of Pathology is the predominantly male population of the various branches of the Armed Forces and Veterans Administration; therefore, sex distribution was biased. Approximately equal distribution of the sexes, with perhaps a slight predominance in men, has been reported by others.

Age Distribution.—The average age of the 35 patients at onset of Bowen's disease was 54 years. The average age at removal or first biopsy was 62 years. The youngest was 38, and the oldest, 87. The age distribution is listed in Table 1.

Duration of Lesions, Number, and Anatomical Sites.—The duration of the lesions from onset to surgery varied from 5 months to 30 years. The average was 7.8 years. The anatomical sites of the lesions are listed in Table 2 and illustrated in Figure 1.

Twenty-two of thirty-five patients had single lesions; seven had clinical evidence of multiple lesions, but only one lesion of each patient was available for microscopic study. All lesions of four other patients were available. Multiple lesions from two patients were available for study, and there was clinical evidence of other lesions which were not submitted for study. The sites and distribution of those lesions clinically similar to Bowen's disease, but not biopsied or surgically removed, were essentially the same as for the known material.

Clinical and Gross Description.—Clinically, the diameters of lesions of 24 patients for whom data were accurate varied from 0.7 to 13 cm.; the median value was 1.9 cm. They usually appeared as erythematous, pigmented, crusty, scaly, fissured, keratotic plaques. Some had heaped-up nodules within the lesion. The configuration varied from round plaques, sharply demarcated from the surrounding tissue, to an irregular, polycyclic, lenticular pattern. A few were ulcerated or eroded. Close inspection of the lesions revealed numerous fragmented hairs protruding from lesions located in hairy areas of the skin. Some lesions were clear in the center; the majority were plaque-like. They were firm, indurated, rough, and granular to palpation. The clinical appearance frequently depended upon the location and other extrinsic factors, such as ex-

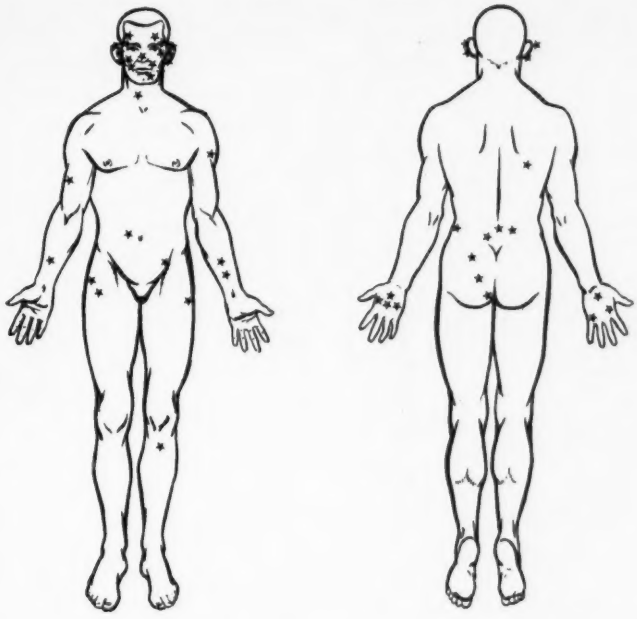


Fig. 1. — Anatomical sites of Bowen's disease with material available for microscopic study.

posure, irritation, treatment, and trauma (Figs. 2 and 3).

The first lesion biopsied or surgically removed from each of the 35 patients was clinically diagnosed under a variety of terms, as follows: squamous-cell carcinoma, 6; basal-cell carcinoma, 4; carcinoma and superficial epitheliomatosis, 3 each; keratosis, senile keratosis, precancerous keratosis, mole or nevus, psoriasis, and no diagnosis or just lesion, 2 each, and melanoma, Bowen's disease, hyperkeratosis with carcinoma, pre-

Figure 2

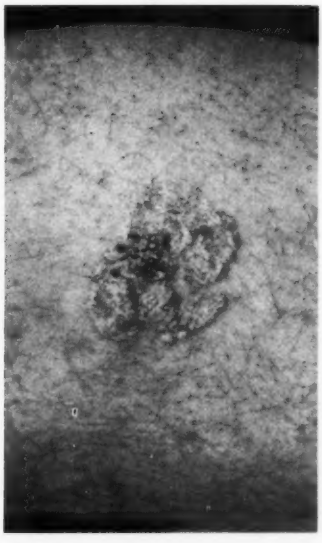


Fig. 2.—Bowen's lesion appearing as a single, scaly, fissured, keratotic, nodular, irregular, plaque-like lesion sharply demarcated from the surrounding tissue.

Fig. 3.—Bowen's disease with multiple coalescing lesions. The lesions varied from erythematous, pigmented, scaly crusted plaques to ulcerated, eroded areas and heaped-up granular nodules. The borders were sharply demarcated from the surrounding tissue. Invasive squamous-cell carcinoma occurred and eventually widespread metastasis.

Figure 3

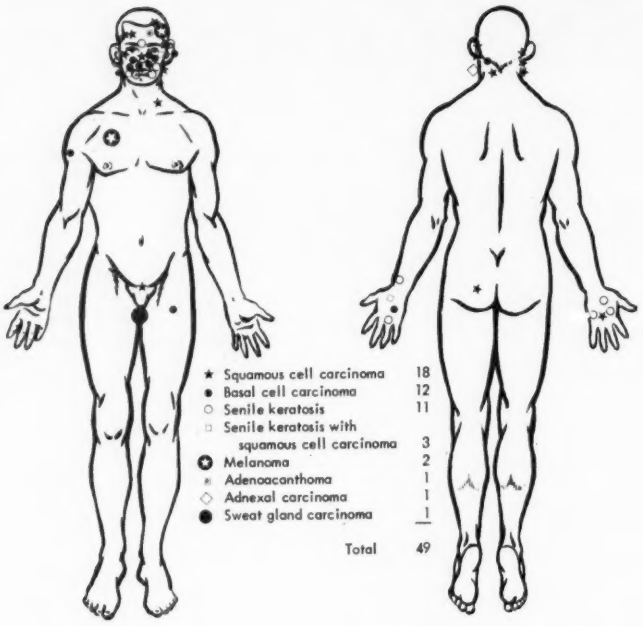

★ Squamous cell carcinoma 18
● Basal cell carcinoma 12
○ Senile keratosis 11
□ Senile keratosis with squamous cell carcinoma 3
✪ Melanoma 2
⊛ Adenoacanthoma 1
◇ Adnexal carcinoma 1
● Sweat gland carcinoma 1
Total 49

Fig. 4.—Locations of all premalignant and malignant skin lesions examined microscopically.

cancerous hyperkeratosis, seborrheic keratosis, lupus vulgaris or chromoblastomycosis, seborrheic dermatitis, and neurodermatitis, 1 each.

Symptoms.—The patients described combinations of ulceration, crusting and scaling of the lesions, and infrequently episodes of bleeding, usually associated with trauma. Some experienced itching, pain when the lesion was pressed, and pain independent of known trauma.

Premalignant and Malignant Skin Lesions.—In addition to Bowen's disease, the group had a variety of premalignant and malignant cutaneous lesions which were available for microscopic study. These included 15 squamous-cell carcinomas, 10 senile keratoses, 9 basal-cell carcinomas, 3 squamous-cell carcinomas occurring in senile keratosis, 2 malignant melanomas, 1 adenoacanthoma, 1 sweat-gland carcinoma, and 1 adnexal carcinoma (Table 3).

Combinations of Bowen's Disease and Other Lesions and Time Relationship.—Seventeen patients were free of premalignant and malignant skin lesions other than Bowen's disease throughout life; however, fourteen of these had malignant lesions of the internal organs. In only one instance did the internal cancer precede the onset of Bowen's disease.

Three other patients reported skin cancers prior to onset of Bowen's disease, but their statements could not be confirmed. Fifteen patients had various combinations of premalignant and malignant cutaneous lesions associated with Bowen's disease. The order of appearance of these lesions in 13 patients was known; Bowen's disease was either the first lesion or appeared concurrently with other cutaneous lesions in 10 patients, or 77%; it was the second lesion in 3, or 23%. The combinations of lesions and the order of their appearance in relation to Bowen's disease are listed in Table 4, and case summaries, in Table 5.

Latent Period for Premalignant and Malignant Skin Lesions.—Latent periods from onset of Bowen's disease to onset of 39 premalignant and malignant lesions of the skin varied from concurrent onset to 33 years. Breakdown for the average latent

TABLE 3.—*Location of Premalignant and Malignant Skin Lesions on Which Material Was Available for Microscopic Study*

Diagnosis and Location	No. *
Squamous-cell carcinoma	
Ear region	7
Temple	1
Nose	1
Forehead	1
Scalp	1
Neck	2
Hand, dorsum	1
Buttock	1
	(15)
Senile keratosis	
Hand, dorsum	4
Ear	2
Cheek	2
Nose	1
Lip	1
	(10)
Basal-cell carcinoma	
Cheek	2
Mouth area	2
Ear (metatypical or basosquamous)	1
Ear region	1
Alar region	1
Deltoid area (multicentric)	1
Hand, dorsum	1
	(9)
Senile keratosis with squamous-cell carcinoma	
Cheek	2
Hand, dorsum	1
	(3)
Adeno-acanthoma	
Forehead	1
Sweat-gland carcinoma	
Scrotum	1
Adnexal carcinoma	
Neck	1
Malignant melanoma	
Temporal scalp region	1
Chest	1
	(2)
Total lesions	42

* Seven microscopically examined lesions are omitted from this table because the material was not available for our review. These are included in Figure 4. Three each were squamous-cell and basal-cell carcinoma, and one, senile keratosis.

TABLE 4.—*Combinations and Time Relations Between Bowen's Disease and Premalignant and Malignant Cutaneous Lesions*

	No.
Bowen's as First Lesion	
Basal-cell carcinoma	1
Squamous-cell carcinoma	2
Senile keratosis	1
Multicentric basal-cell carcinoma; basal-cell carcinoma	1
Sweat-gland carcinoma	1
	(6)
Bowen's Concurrent (within 1 yr.) with	
Basal-cell carcinoma	1
Senile keratosis, adeno-acanthoma, senile keratosis with squamous-cell carcinoma	1
Squamous-cell carcinoma, senile keratosis, & senile keratosis with squamous-cell carcinoma	1
Basal-cell carcinoma; senile keratosis; squamous-cell carcinoma	1
	(4)
Bowen's as 2d Lesion	
Adnexal carcinoma	1
Basal-cell carcinoma, metatypical; squamous-cell carcinoma; senile keratosis	1
Senile keratosis with squamous-cell carcinoma; basal-cell carcinoma; squamous-cell carcinoma; senile keratosis; adnexal carcinoma	1
	(3)
Time relation of Bowen's unknown	
Senile keratosis	1
Basosquamous or metatypical basal-cell carcinoma	1
	(2)
Total patients	15

periods for the various types of lesions in relation to the onset of Bowen's disease is as follows: 3 years each for sweat-gland carcinoma and adnexal carcinoma; 5.6 years for basal-cell carcinoma; 5.8 years for squamous-cell carcinoma; and 9.5 years for senile keratosis. The lesions of adeno-acanthoma and squamous-cell carcinoma occurring in senile keratosis were few in number and had occurred before the Bowen's lesion, so no time relationship averages could be established. Two lesions of malignant melanoma (primary site unknown) occurred in one patient 14 years after onset of the Bowen's lesion. The average for the entire group was 6.2 years (Table 5).

The curves of Chart 1 are cumulative percentages and depict the patient-years from onset of Bowen's disease to onset of malignant and premalignant cutaneous lesions. The median latency period of each of the cutaneous lesions is that point where the particular curve is intercepted by the 50% value. The median latency periods are between the sixth and seventh years for basal-cell carcinoma, squamous-cell car-

TABLE 5.—*Summary of Case Data*

Site of Cancer & Case No.	Death				Onset		Cutaneous Premalignant & Malignant Lesions with Latent Period, Yr.			Systemic Manifestations & Latent Period, Yr.		
	Age	Yr.	Race	Sex	Age	Yr.	Latent Period *		Diagnosis †	Latent Period ‡	Primary §	Metastasis ‖
Group I: Patients with Internal Cancer												
Respiratory												
1	48	1954	W	M	47	1953	0	1952	Adenoacanthoma, forehead †; senile keratosis with sq. cell ca., cheek †	1	1954 Epidermoid ca., right lung	Left lung, liver, thoracic duct, intestine, mesenteric l. n.
							0	1953	Senile keratosis, dorsum of hand †			
2	63	1949	W	M	58	1944	--	--	--	4	1948 Bronchogenic ca., undifferentiated, left lung	Right lung
3	71	1955	W	M	45	1929	--	--	Senile keratosis, wrist, therapy 1951	26	1955 Sq. cell ca. larynx & hypopharynx; adenocarcinoma prostate §	Mediastinum, cervical l. n.
4	68	1954	W	M	47	1933	--	--	--	11	1944 Sq. cell ca., larynx	Left lung, brain
5	55	1951	W	M	40	1936	--	--	"Skin cancer," temple; therapy 1937	15	1951 Bronchogenic ca., differentiated, right lung	Mediastinum, brain
							--	--	"Skin cancer," forehead; therapy 1937			
							--	--	"Skin cancer," temple; therapy 1944			
6	76	1953	W	M	73	1950	--	--	"Skin cancer," ear; therapy 1936	2	1952 Bronchogenic ca., right lung	Left lung, heart, mediastinal l. n., subcutaneous tissue left axilla
							--	--	"Skin cancer," both temples; therapy 1940			
							--	--	"Skin cancer," dorsum of hand; therapy 1946			
7	64	1954	W	M	58	1948	0	1948	Basal-cell ca., cheek †	6	1954 Bronchogenic ca., undifferentiated, left lung	Brain, liver, adrenals, left pleura, left brachial plexus
											1954 Malignant thymoma	
8	60	1956	W	M	58	1954	--	--	--	2	1956 Bronchogenic ca., undifferentiated, right lung §	Metastasis present, locations, n. s.
Gastrointestinal												
9	67	1951	W	M	54	1938	--	--	--	13	1951 Adenocarcinoma, stomach §	Gastrohepatic l. n., peripancreatic l. n., lung
10	63	1954	W	M	53	1943	--	--	--	11	1954 Adenocarcinoma, stomach	Liver, peritoneum, omentum, abdominal l. n.
11	47	1950	W	M	37	1940	--	--	Basosquamous cell, postauric.; therapy 1943	9	1949 Adenocarcinoma, stomach	Omentum, small intestine, abdominal l. n., kidney, bone

12	74	1949	W	M	59	1934	12	1946	Basal-cell ca., deltoid area, multicentric variety †	15	1949	Adenocarcinoma, stomach	Abdominal wall
							14	1948	Basal-cell ca., thigh				
13	62	1949	W	M	47	1934	5	1939	Sq.-cell ca., penis	14	1948	Squamous-cell ca., esophagus	Trachea, regional l. n., lungs, bilateral, mediastinum, stomach, thoracic vertebrae
Genitourinary													
14	77	1947	W	M	73	1943	--	--	"Skin cancer," nose; therapy 1901	4	1947	Papillary ca., urinary bladder	
							1	1944	Basal-cell ca., lip				
15	62	1953	W	M	51	1942	0	1941	Senile keratosis with sq.-cell ca., cheek †	3	1945	Papillary ca., urinary bladder	Lungs, adrenals, liver, spleen, regional l. n., vertebrae, pelvis, thoracic cage
								1948	Basal-cell ca., above mouth †, angle of mouth †, dorsum of hand †; sq.-cell ca. post-infer., ear †, sup. ear †, ant. ear †, nose †				
							7	1949	Senile keratosis, cheek †, nose †, ear †, sq.-cell ca., post. neck †, post. ear †		1953	Adenocarcinoma, prostate §	
							8	1950	Basal-cell ca., cheek †, preauric †				
							9	1951	Sq.-cell ca., postauric. †; adnexal ca., neck †; basal-cell ca. recurrent preauric †				
							10	1952	Sq.-cell ca., below ear †				
16	43	1956	W	M	33	1946	--	--	--	10	1956	Adenocarcinoma, prostate	Lung, pleura, liver, spleen, pancreas, adrenals, vertebrae
17	73	1955	W	M	71	1953	--	--	--	2	1955	Adenocarcinoma, prostate §	
18	61	1955	W	M	58	1952	--	--	--	3	1955	Renal-cell ca., kidney §	Lung, heart, rib
											1955	Adenocarcinoma, prostate §	
Reticuloendothelial													
19	53	1950	W	M	47	1944	--	--	--	2	1946	Lymphosarcoma, cervical l. n.	Generalized
20	73	1953	W	M	69	1949	--	--	"Skin cancer," dorsum of hand; therapy 1947	4	1953	Leukemia, chronic myelogenous	Generalized
21	64	1955	W	M	59	1950	0	1947	Adnexal ca., nose	0	1950	Leukemia, chronic lymphocytic	Generalized
22	65	1956	W	M	61	1952	--	--	--	0	1951	Lymphosarcoma	Generalized
Cutaneous													
23	65	1939	W	F	62	1936	--	--	Sq.-cell ca., buttock; therapy 1937 †	3	1939	Squamous-cell ca., left chest & neck	Adrenals, heart, ovaries, rib, regional l. n., mesenteric l. n., mediastinal l. n.
24	55	1953	W	M	41	1939	0	1939	Basal-cell ca., alar region †	14	1953	Malignant melanoma, left temporal scalp region and chest, primary unknown †	Suprarenal glands, lungs, brain, skin
							4	1943	Senile keratosis, lip †				

TABLE 5.—*Summary of Case Data*—Continued

Site of Cancer & Case No.	Death				Onset		Cutaneous Premalignant & Malignant Lesions with Latent Period, Yr.			Systemic Manifestations & Latent Period, Yr.			
	Age	Yr.	Race	Sex	Age	Yr.	Latent Period *		Diagnosis †	Latent Period ‡		Primary §	Metastasis ‖
							--	1949	Recurrent ca., alar region †				
							--	--	Sq.-cell ca., neck †				
							--	--	Sq.-cell ca., temple †				
							--	--	"Skin cancer," neck & temple; therapy 1950				
							--	--	"Skin cancers" neck, † therapy 1951				
							12	1951	Sq.-cell ca., scalp †				
								1952	Recurrent sq.-cell ca. preauric. †				
25	61	1947	W	M	50	1936	--	--	--	10	1946	Bowen's disease with sq.-cell ca., right thigh, inguinal region, buttock & perineum	Bladder wall, colon, liver, right lung, pelvic tissues, regional l. n.
26	60	1952	W	M	25	1917	--	--	--	30	1947	Bowen's disease with sq.-cell ca., right thigh	Inguinal l. n.
Breast													
27	74	1952	W	F	68	1946	--	--	--	3	1949	Adenocarcinoma, left breast	Regional l. n., heart, lungs, skin, stomach, bone
Endocrine													
28	60	1952	W	F	38	1930	--	--	--	21	1951	Papillary adenocarcinoma, right ovary	Parietal & visceral peritoneum of pelvic & abominal cavity (found at oper.)

Group II: Patients with No Internal Cancer

										Latent Period ‡	Description, Yr.	
1	89	1946	W	M	73	1930	3	1933	Sweat gland ca., scrotum †	16	1946	Myocardial failure following aneurysm, dissecting & saccular, thoracic & abdominal aorta
							--	--	"Skin cancer," finger; therapy 1936			
							--	--	"Skin cancer," nose; therapy 1936			
							--	--	"Skin cancer," buttock; therapy 1938			
							--	--	"Skin cancer," ear; therapy 1938			
							--	--	"Skin cancer," shoulder; therapy 1940			
							--	--	Multiple "skin cancers," shoulders, upper extremities, trunk; therapy 1944			

2	59	1949	W	M	24	1914	9	1923	Senile keratosis, dorsum of hand †	35	1949	Coronary thrombosis with myocardial infarction; cerebral thrombosis
							26	1940	Senile keratosis, ear †			
							33	1947	Senile keratosis, cheek †			
3	76	1948	W	M	75	1947	0	1947	Sq.-cell ca., forehead †	1	1948	Cerebral vascular accident, arteriosclerotic rupture of aortic arch & thoracic aorta; terminal gastric hemorrhage
							--	--	Senile keratosis, dorsum of hand †			
							--	--	Senile keratosis with sq.-cell ca., hand †			
4	68	1955	W	M	51	1938	--	--	--	17	1955	Myocardial infarction, old & recent; arteriosclerosis & thrombosis, coronary arteries
5	59	1956	W	M	55	1952	0	1951	Basal-cell ca., metatypical, ear region †	4	1956	Shock due to perforated wall of the stomach & generalized peritonitis; bronchopneumonia
							1	1953	Sq.-cell ca., dorsum of hand †			
							2	1954	Senile keratosis, dorsum of hand †			
6	60	1956	W	M	54	1950	--	--	--	6	1956	Complications following resection of small intestine & right colon & right transverse colon for mesenteric thrombosis; acute & chronic ulcers of the colon; arteriosclerosis of the aorta with ulceration & mural thrombosis; acute cholangiolitis; acute renal tubular necrosis; acute bronchopneumonia
7	68	--	W	M	68	--	--	--	--	0	1955	Myocardial infarction, secondary to thrombotic occlusion; fibrosis, myocardium with aneurysmal dilatation left ventricle; adhesive pericarditis

* From onset of Bowen's disease to occurrence of cutaneous premalignant or malignant lesions.
† Diagnoses were made from slides received for study.
‡ From onset of Bowen's disease to detection of internal cancer or death from other causes.
§ Found at autopsy.
‖ L. n. indicates lymph node.

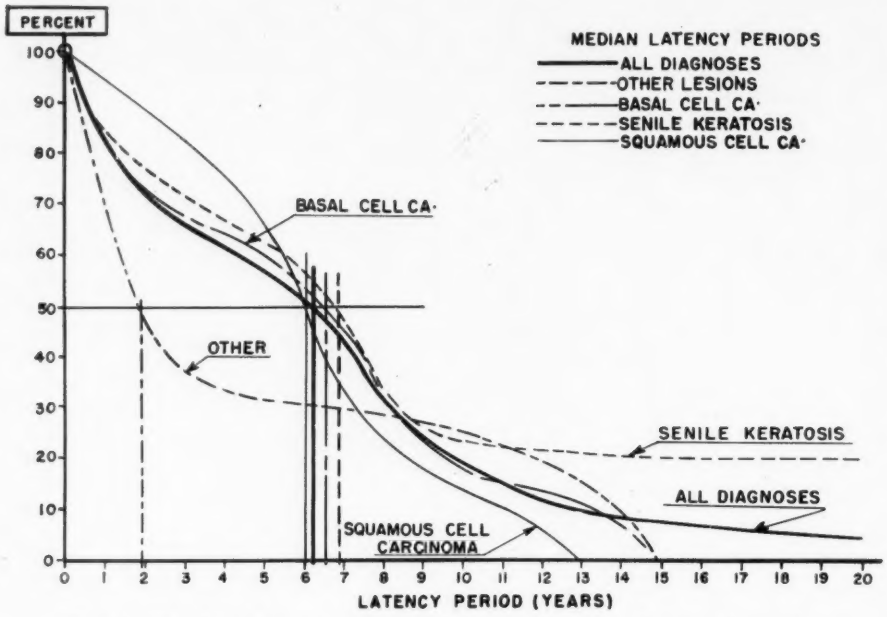


Chart 1.—Time lapse from onset of Bowen's disease to onset of malignant and premalignant cutaneous lesions, by diagnosis.

cinoma, senile keratosis, and for all diagnoses; however, for lesions other than the foregoing, the median latency period is approximately two years.

Primary Internal and Metastasizing Primary Cutaneous Cancers.—Twenty-eight of the thirty-five patients had cutaneous and systemic cancers which either directly or indirectly contributed to their terminal illness. The number, primary locations, and types of these malignant tumors were as follows: eight respiratory, including squamous-cell carcinoma of the hypopharynx, larynx, and lung, and bronchogenic carcinoma; five gastrointestinal, including squamous-cell carcinoma of the esophagus and adenocarcinoma of the stomach; five genitourinary, including renal-cell carcinoma, papillary carcinoma of the urinary bladder, and adenocarcinoma of the prostate; four reticuloendothelial, including lymphosarcoma, chronic myelogenous leukemia, and chronic lymphocytic leukemia; four cutaneous, including metastasizing squamous-cell carcinoma, squamous-cell carcinoma occurring in Bowen's disease with subsequent metastasis, and malignant melanoma; one endocrine tumor diagnosed as papillary adenocarcinoma of the ovary, and one lesion called adenocarcinoma of the breast (Table 5).

Combinations of Systemic Cancers.—There were four examples of combinations of two types of internal malignant lesions, i. e., squamous-cell carcinoma of the hypopharynx and larynx and adenocarcinoma of the prostate; papillary carcinoma of the urinary bladder and adenocarcinoma of the prostate; renal-cell carcinoma and adenocarcinoma of the prostate, and bronchogenic carcinoma and malignant thymoma (Table 5).

The internal malignant tumors in six patients were first detected at autopsy. Twenty-six of the twenty-eight patients had metastatic lesions or generalized spread from their primary tumors.

Seven of the thirty-five patients died without systemic cancer, but four of these had premalignant lesions of senile keratosis or malignant lesions of squamous-cell car-

cinoma occurring in senile keratosis, squamous-cell carcinoma, basal-cell carcinoma, or sweat-gland carcinoma.

Supplementary Data.—Primary internal malignant lesions were reported on follow-up of 23 of more than 100 living patients with Bowen's disease. The pathologic diagnoses were as follows: two each with adenocarcinoma of the rectum, squamous-cell carcinoma of the mucous membrane of the lip, squamous-cell carcinoma of the tongue, bronchogenic carcinoma, and adenocarcinoma of the prostate; one each with carcinoma of the mucous membrane of the anus, adenocarcinoma of the colon, adenocarcinoma of the stomach, epidermoid carcinoma of the nasopharynx, epidermoid carcinoma of the hard palate, squamous-cell carcinoma of the cornea and conjunctiva, carcinoma of the kidney, papillary carcinoma of the bladder, squamous-cell carcinoma of the urethra, adenocarcinoma of the uterus, chronic lymphatic leukemia, follicular lymphoma, and adenocarcinoma of the thyroid.

Latent Period for Malignant Internal Lesions.—The latent period from onset of the Bowen's disease until detection of a malignant internal lesion or a metastasis from a cutaneous cancer was from concurrent onset to 35 years. The average was 8.5 years. The average time relationship from onset of Bowen's disease until detection of malignant lesions in the various systems is as follows: 1.3 years, reticuloendothelial; 4.5 years, genitourinary tract; 8.4 years, respiratory system; 12 years, endocrine and endocrine-influenced systems; 13 years, gastrointestinal tract, and 14.2 years, skin (Table 5).

Since individual variations affect the averages, Chart 2 is presented to indicate the time intervals from onset of Bowen's disease to the detection of malignant lesions in each system. Fifty per cent of the lesions of the genitourinary tract had been detected within 4 years and of those of the gastrointestinal tract within 14 years.

Follow-Up Period and Survival Time.—The follow-up period from first diagnosis of the Bowen's lesion until death ranged from 13 days to 14 years; the average was 3.4 years. Ten patients died in less than 1 year; twelve, in less than 2 years; nineteen, in less than 3 years; twenty-three, in less than 4 years; twenty-six, in less than 5 years; nine survived beyond 5 years, but all had died by the end of a 14-year period.

Family History.—Information was obtained from records of 22 patients regarding internal malignant tumors in their relatives. Eight families (36%) had internal cancer. One patient whose father had carcinoma of the bladder also had a brother whose skin was sensitive to sunlight and had skin cancers.

Past History of Patients.—Only one patient was known to have received arsenical therapy. Neoarsphenamine had been administered five years before onset of a single lesion of Bowen's disease on the left

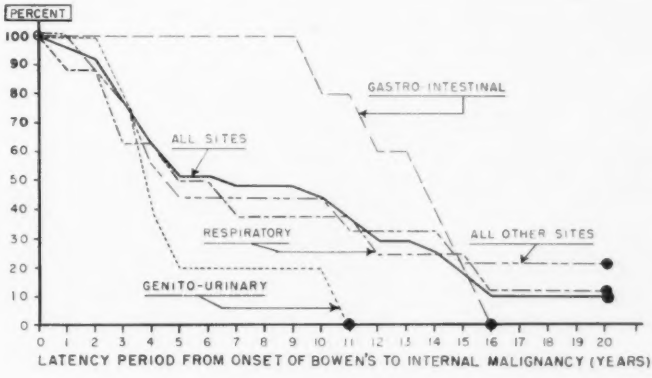


Chart 2.—Rate of development of internal malignancy with reference to onset of Bowen's disease, by anatomic site.

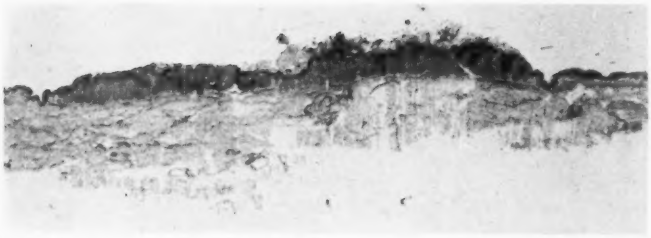


Fig. 5.—Bowen's lesion with plaque-like acanthosis, hyperkeratosis, and parakeratosis. Reduced about 5% from mag. × 9.

temple. Since the clinical histories as a group were adequate, it seems likely that this is the only patient who had contact with arsenical compounds.

Treatment and Results.—Methods of treatment of the 48 lesions of Bowen's disease in the 35 patients included topical therapy, surgical excision and grafting, x-ray, radium, desiccation, and curettement. No lesions were cured or altered by local therapy. Six were treated with cancericidal doses of x-ray; one of these recurred, and four were completely unaltered, as proved by follow-up biopsies after treatment. The sixth lesion was treated with a combination of desiccation and curettement followed by x-ray, with no recurrence 18 months later. Lesions of two other patients were treated with therapeutic doses of radium, and both were apparently cured. Two were treated by desiccation, curettement, or both, and both recurred. Six of thirty-six lesions recurred after surgical excision. Subsequently, the nine lesions that recurred were treated a second time—seven with surgical excision, one with x-ray, one with desiccation and/or curettement. The one treated by desiccation and/or curettement recurred. Five of the lesions treated were still present terminally. Terminal examination of the skin of the deceased patients revealed that nine had evidence of untreated lesions clinically similar to Bowen's disease.

Microscopic Examination

Sections from the lesions of Bowen's disease were stained with hematoxylin and eosin. Examination under the scanning and low-power objective revealed a plaque-like lesion with hyperkeratosis, parakeratosis, or both, and acanthosis. Under higher power, atypical epithelial proliferation, with loss of normal architecture and "windblown" appearance, was striking. Cellular atypism in the form of multinucleated giant cells, vacuolated cells, and mitotic figures occurred at all levels throughout the epidermis. The nuclei of the atypical epithelial cells varied in size and shape but were generally enlarged and hyperchromatic, with prominent nucleoli. Near the surface, some nuclei were shrunken and surrounded by a clear halo. Occasionally, individually keratinized or dyskeratotic cells occurred in all layers. Inflammatory cells, mostly lymphocytes and plasma cells, usually infiltrated the corium near the base of the lesion. The intensity of the inflammatory infiltrate was variable in the same lesion as well as between lesions.

Forty-eight lesions of Bowen's disease from the 35 patients were examined microscopically. Four (11%) of the 35 patients had lesions in which there was microscopic evidence of invasion as squamous-cell carcinoma. In two (5.7%) the lesions invaded deeply, and both patients had metastasis (Figs. 5-10).

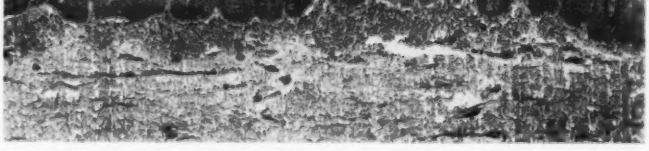


Fig. 6.—Plaque-like lesion with hyperkeratosis, parakeratosis, acanthosis, and no evidence of invasion of the corium. Reduced about 5% from mag. × 48.

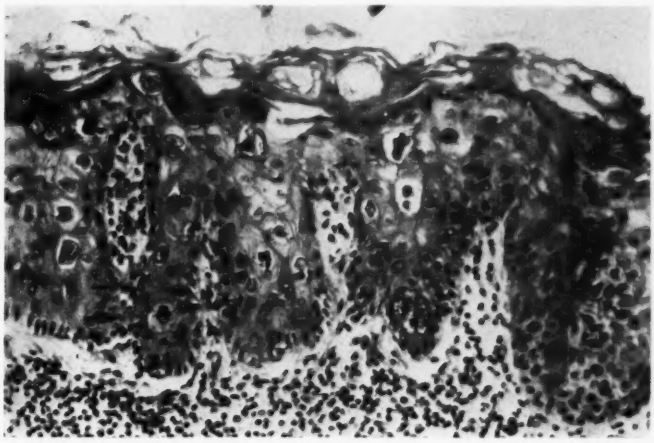


Fig. 7. — Area from Figure 6. There is loss of normal architecture and cellular atypism in the form of multinucleated cells, vacuolated cells, and mitotic figures at all levels of the epidermis. An inflammatory infiltrate of lymphocytes and plasma cells is seen in the upper corium. Reduced about 5% from mag. × 185.

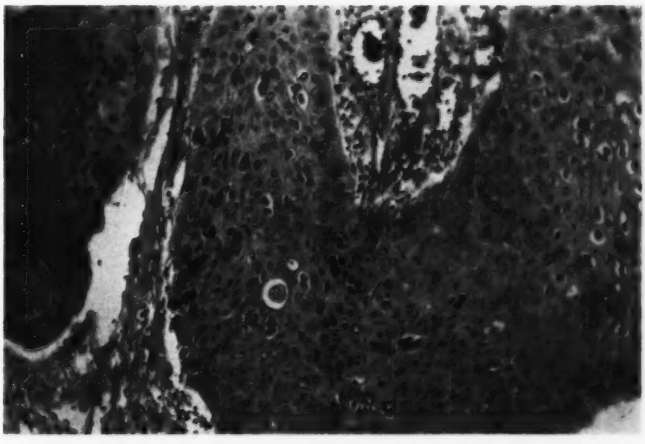


Fig. 8.—High power of a Bowen's lesion with "windblown" appearance, abnormal cells, mitotic figures, and individual cell keratinization. Reduced about 5% from mag. × 305.

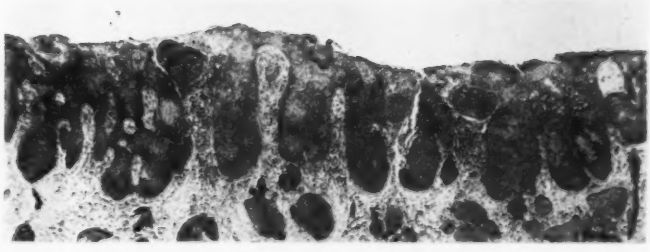


Fig. 9.—Plaque-like lesion of Bowen's disease invading as squamous-cell carcinoma. Reduced about 5% from mag. × 48.

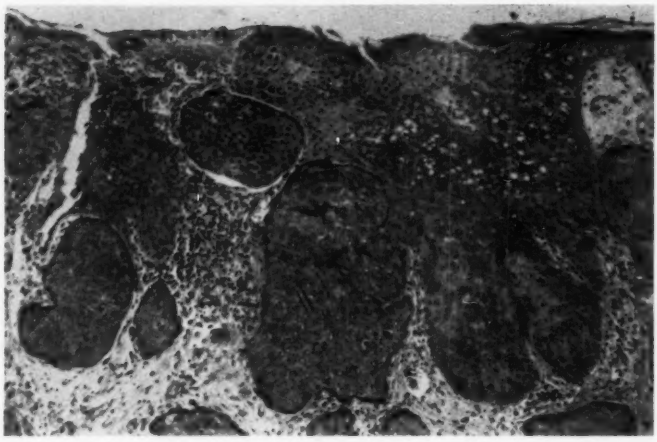


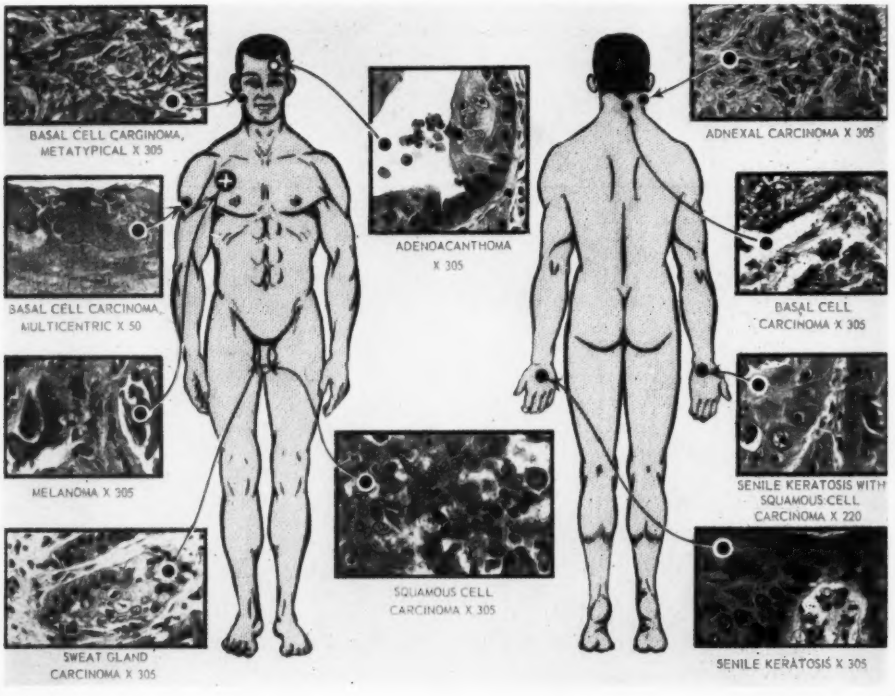
Fig. 10.—High power of Figure 9. Squamous-cell carcinoma eventuating in widespread metastasis and death of the patient. Reduced about 5% from mag ×102.

Hematoxylin-and-eosin-stained sections were examined on all cutaneous premalignant and malignant lesions, as well as those of internal organs. (Figures 11 and 12 show the types of various cutaneous and internal lesions.)

Controls

In view of the tendency of this group of people with Bowen's disease to have cutaneous lesions of senile keratosis and squamous-cell carcinoma, we examined

Fig. 11.—Types of premalignant and malignant skin lesions.


BASAL CELL CARGINOMA, METATYPICAL X 305
BASAL CELL CARCINOMA, MULTICENTRIC X 50
MELANOMA X 305
SWEAT GLAND CARCINOMA X 305
ADENOACANTHOMA X 305
SQUAMOUS CELL CARCINOMA X 305
ADNEXAL CARCINOMA X 305
BASAL CELL CARCINOMA X 305
SENILE KERATOSIS WITH SQUAMOUS CELL CARCINOMA X 220
SENILE KERATOSIS X 305

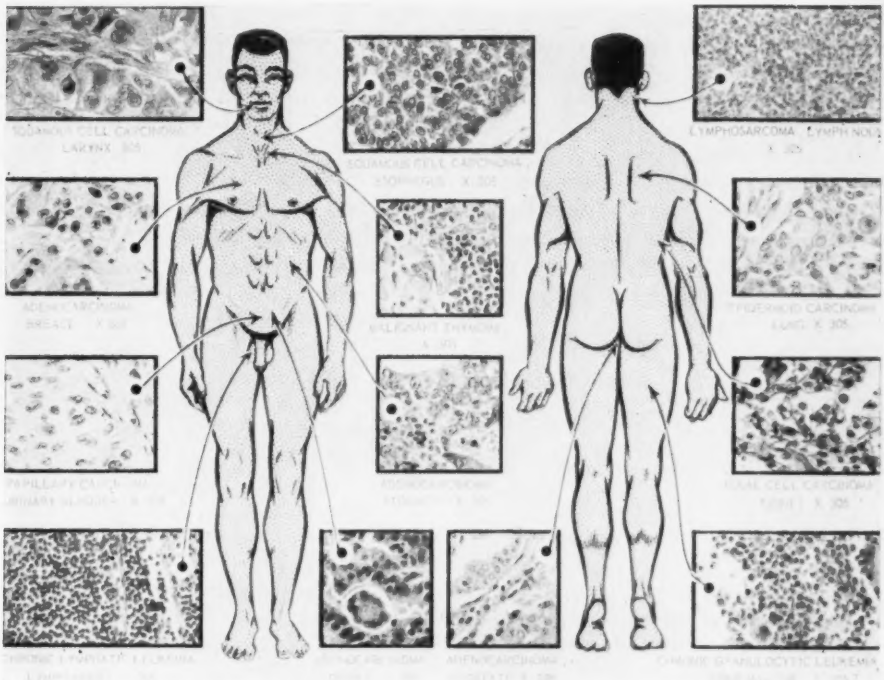


Fig. 12.—Types of internal cancer.

microscopically surgical specimens and autopsy material from deceased persons with these diseases. Material from persons with exfoliative dermatitis was also examined, since this disease is reportedly associated with internal cancer and not with cutaneous malignant lesions. The control groups here discussed were unselected with respect to race and sex; however, for purposes of statistical testing (Table 6), only the white men 43 years of age and older were utilized, because the varying proportions of women, Negroes, or white men under 43 years of age did not permit valid testing with these categories included.

Senile Keratosis.—Material was examined microscopically from 35 patients with lesions of senile keratosis surgically removed prior to death or obtained at autopsy. The material was chosen at random.

TABLE 6.—*Internal Cancers in White Males Forty-Three Years of Age and Over with Bowen's Disease Compared to Those in Control Groups*

Diagnosis	No.			% in Group				
	Internal Cancer	No Internal Cancer	Total	Internal Cancer	No Internal Cancer	χ^2	Degrees of Freedom	Probability Value
Bowen's disease *	22	7	29	76	24	5.7442	1	0.01
Squamous-cell carcinoma, skin	9	12	21	43	57			
Bowen's disease	22	7	29	76	24	1.2484	1	0.30
Senile keratosis	22	13	35	63	37			
Bowen's disease	22	7	29	76	24	28.3371	1	0.0005
Exfoliative dermatitis	5	35	40	12	88			

* Some of these had squamous-cell carcinoma, but none had metastasis from skin lesions.

All the patients were Caucasian men. The average age at onset was 62 years and at surgical removal or autopsy, 64 years; the range was from 38 years to 86 years. The duration of the lesions from onset to removal varied from 1 month to 10 years; the average duration was 1.8 years. All the lesions were anatomically located on exposed parts of the body; the dorsum of the hand, forearm, neck, nose, ear, cheek, forehead, and eyelid. Twenty-two (63%) of the thirty-five patients with senile keratosis had primary internal cancers, the majority of which were either directly or indirectly responsible for their deaths. The types and locations were, in order of frequency: bronchogenic carcinoma, nine; adenocarcinoma of the prostate, five; renal-cell carcinoma, papillary carcinoma of the bladder, follicular lymphoblastoma, generalized reticulum-cell lymphosarcoma, adenocarcinoma of the stomach, and malignant carcinoid of the ileum, one each, and combinations of chronic lymphocytic leukemia and Hodgkin's disease and of chronic granulocytic leukemia and adenocarcinoma of the colon, one each. Ten of the thirty-five patients with senile keratosis also had basal-cell carcinoma of the skin. Obviously, none of these lesions metastasized. The patients with senile keratosis did not have any lesions which were either clinically or histologically similar to Bowen's disease.

Squamous-Cell Carcinoma of the Skin.—Thirty-five patients with primary squamous-cell carcinoma of the skin were studied. There were 31 white men, 2 Negro men, and 2 white women. Their ages at removal of the lesions ranged from 25 years to 93 years. The average age at onset was 64 years and at surgical removal or autopsy, 66 years. The duration from onset to biopsy or surgical removal varied from 1 month to 11 years, with an average of 1.9 years. Anatomically, the lesions were located on the head, neck, trunk, and extremities. Ten (28.6%) of the thirty-five had primary internal cancers which contributed to their deaths. Two of these also had metastasis from cutaneous squamous-cell carcinomas, and each had a second internal primary malignant lesion, adenocarcinoma of the prostate, and bronchogenic carcinoma, respectively. Six had single internal malignant lesions, which included one each with epidermoid carcinoma of the lung, squamous-cell carcinoma of the pharynx, carcinoma of the pancreas, adenocarcinoma of the prostate, generalized lymphosarcoma, and adenocarcinoma of the stomach. Two patients had adenocarcinoma of the prostate; each had a second primary lesion of squamous-cell carcinoma of the larynx and adenocarcinoma of the rectum. Thirteen (37%) died as a result of metastasis from squamous-cell carcinomas of the skin; twelve patients died from other causes. Twenty-three (65.7%) died of metastasis from squamous-cell carcinoma of the skin or from primary internal cancer.

Exfoliative Dermatitis.—Clinical data and pathologic materials diagnosed as exfoliative dermatitis were available from 139 patients. Four of ninety-five autopsied patients had primary malignant lesions of internal organs. Three patients who were alive at last report had primary internal cancer. The type and sites of internal cancer were as follows: Two had Hodgkin's disease, and one each had mycosis fungoides, chronic lymphocytic leukemia, adenocarcinoma of the stomach, adenocarcinoma of the liver, and adenocarcinoma of the prostate. Thus, 7 (5%) of the 139 patients had primary internal cancers associated with the exfoliative dermatitis.

This group, drawn from the 139 patients with exfoliative dermatitis for comparison with the patients with Bowen's disease, consisted of all white men 43 years and over for whom autopsy material was available, and all those living for whom surgical material showed the presence of internal cancer. There were 40 such men—38 with autopsy and 2 with surgical material. Of these forty, five (12%) had internal cancer.

Comparative Studies

The following lesions and diseases were studied for possible association with internal

TABLE 7.—*Internal Cancer and Metastasis from Cutaneous Cancer, Bowen's Disease, and Diseases Selected for Comparison*

Diagnosis	Total No.*	Primary Internal Cancer		Metastasis from Cutaneous Cancer	
		No.	%	No.	%
Bowen's disease	35	24	68.6	4	11.4
Senile keratosis	35	22	63.0	—	—
Acanthosis nigricans	19	10	52.6	—	—
Herpes zoster	43	15	34.8	—	—
Squamous-cell carcinoma (cutaneous)	35	10†	28.6	13	37.1
Extramammary Paget's disease	23	3	13.0	3	13.0
Dermatomyositis	45	7	15.6	—	—
Arsenical keratosis	15	2	13.3	2	13.3
Paget's disease of the breast	40	2	5.0	—	—
Poikiloderma atrophicans vasculare (Jacobi)	10	1	10.0	—	—
Kaposi's sarcoma	50	3	6.0	—	—
Exfoliative dermatitis	139	7	5.1	—	—
Xeroderma pigmentosum	8	—	—	3	37.5
Erythroplasia of Queyrat	24	—	—	—	—

* Total number in each group equals 100%.

† Two of these patients had metastasis from cutaneous squamous-cell carcinoma.

cancer, and comparative data for both these and the control groups are shown in Table 7.

Arsenical Keratosis.—Among 15 patients with keratosis and a definite history of ingestion or contact with arsenic, 5 were dead. Three (60%) of these had either metastasis from malignant lesions of the skin or primary internal cancer; in two instances the metastasis was from squamous-cell carcinoma of the feet and hand, respectively, which eventually caused death. The third patient died of carcinoma of the ampulla of Vater, with metastasis to the liver and regional lymph nodes. The remaining two patients died from cardiovascular and respiratory diseases. One of the ten patients still alive at last report is a 77-year-old white woman, who at present is two and one-half years postoperative for adenocarcinoma of the right breast.

The types of arsenic were as follows: Fowler's solution, 11 patients; arsenate of lead and arsenous acid, 1 each; an injectible and an oral arsenical compound, 2. The patients received the arsenical preparations for diseases such as psoriasis, neurodermatitis, acne, bronchial asthma, chorea, migraine, epilepsy, and rheumatic fever. One patient was exposed to arsenic in sprays, by eating apples and drinking well water contaminated with arsenate of lead. Histologically, the majority of the lesions of arsenical keratosis were practically indistinguishable from those of Bowen's disease.

Erythroplasia of Queyrat.—Twenty-four white male patients with typical penile lesions were studied. Eight died; none had internal cancers on the basis of follow-up data and material available for study. Six patients had microscopic evidence of local invasion, but none had evidence of metastasis to regional lymph nodes. None of the 24 had lesions of Bowen's disease on the skin or other premalignant or malignant cutaneous lesions. Microscopically, erythroplasia of Queyrat resembles Bowen's disease of the skin.

Paget's Disease of the Breast.—Neubecker[5] reviewed material from 46 female patients with this disease. Surgical tissues from 40 patients were available for gross and microscopic examination; in 38 (95%) underlying carcinoma of the breast was found. Follow-up data revealed that four of these patients also had primary carcinoma of the opposite breast and one had an adenocarcinoma of the sigmoid colon. A fifth patient had an abdominal perineal resection for malignant tumor of unknown type, in addition to surgery for carcinoma of the breast. At last report, 5 of the 40 were dead, all of widespread metastasis from the breast. Although the follow-up is not complete, it appears possible that at least 5% of patients with Paget's disease of the breast might have primary internal malignant lesions in addition to breast carcinoma.

Extramammary Paget's Disease.—We reviewed material from 23 adult patients with this disease. Twelve were female and eleven male. The lesions were located on the labia, anus, penis, scrotum, suprapubic region, groin, and axilla. Five patients had under-

lying adnexal carcinoma of the skin; three of these also had metastasis to the regional lymph nodes. Two patients had adenocarcinoma of the rectum, of which one died. One woman died as a result of widespread metastasis from a primary mucinous adenocarcinoma of the urethra. A total of eight patients, or 35% of those with lesions of extramammary Paget's disease, had either an underlying primary internal cancer or an adnexal carcinoma of the skin. Patients with internal cancer comprised 13% of the group, while 13% had metastasis from the skin to the regional lymph nodes.

Kaposi's Sarcoma.—Fifty patients with this disease entity were studied by Cox and Helwig.[6] Forty-seven had skin manifestations of the disease. Three also had chronic lymphocytic leukemia, mycosis fungoides, or Hodgkin's disease. The two latter diseases occurred simultaneously with Kaposi's sarcoma. Six per cent of patients with Kaposi's sarcoma also had a malignant lymphoma.

Xeroderma Pigmentosum.—Material from eight patients with xeroderma pigmentosum was reviewed. The sexes were equally divided; the ages ranged from 12 to 42 years. Three were dead as a result of metastasis from squamous-cell carcinoma of the skin to internal organs. Four of the five living patients had a variety of premalignant and malignant cutaneous lesions. None of the eight was known to have a primary internal cancer.

Carcinoid.—Manion and Helwig[7] reviewed material diagnosed as carcinoid from 321 patients and found that 17 (5.3%) had systemic and cutaneous manifestations of the malignant carcinoid syndrome.

Dermatomyositis.—Forty-five patients with this disease were studied. Five (25%) of twenty known dead were found to have the following primary internal cancers: Hodgkin's disease, multiple myeloma, carcinoma of the kidney, adenocarcinoma of the ovary, and squamous-cell carcinoma of the nasopharynx. The remaining 25 patients, who were alive at last report, include 2 women who were postoperative for carcinoma of the cervix and for carcinoma of the breast. Sixteen per cent were known to have primary internal cancers.

Poikiloderma Atrophicans Vasculare (Jacobi).—Clinical histories and biopsy material of 10 adult patients were considered acceptable for this diagnosis. All of the patients were alive at last report, and only one, a white woman, had mycosis fungoides.

Herpes Zoster.—Material from 43 patients with this disease was examined. Fifteen (35%) were known to have internal cancers: five of these with Hodgkin's disease; three with bronchogenic carcinoma; two with chronic lymphatic leukemia; one each with chronic myelogenous leukemia, multiple myeloma, carcinoma of the thyroid, and adenocarcinoma of the head of the pancreas, and one with an unclassified malignant tumor and widespread metastasis to bones. The onset of the herpes zoster was during the time the 15 patients had their internal malignant lesions. Nineteen (44%) were dead, and fourteen had died of primary internal cancers.

Three of the thirty-five patients with Bowen's disease (not included in above group) had herpes zoster, associated in each instance with internal cancers; one each had adenocarcinoma of the prostate and lymphosarcoma, and one patient had carcinoma of both kidney and prostate.

It must be emphasized that much of our material on herpes zoster came from dying patients debilitated with internal cancer and as a group more susceptible to infection. This factor probably accounts for the high incidence of association in the group and does not necessarily imply a true relationship between the occurrence of herpes zoster and internal cancer or any specific type of malignant tumor.

Acanthosis Nigricans.—Nineteen patients with acanthosis nigricans were studied. Their types were classified as malignant or benign on the basis of clinical histories, follow-up data, and histologic material. Ten (52.6%) were classified as malignant; nine, as benign. Nine of the ten patients were

known to be dead and either at surgery or autopsy were noted to have the following internal malignant lesions: Five had adenocarcinoma of the stomach; one each had adenocarcinoma of the liver, adenocarcinoma of the thyroid, bronchogenic carcinoma, and retroperitoneal sarcoma. The 10th patient, a 23-year-old Negro man, is still alive two and one-half years post-treatment for epidermoid carcinoma of the nasopharynx. The nine patients considered as having benign acanthosis nigricans were still alive at last report and on the basis of present information had no detected internal cancers. Histologically, and often clinically, the benign and malignant types of acanthosis nigricans were indistinguishable.

Statistical Comparison

Nineteen (83%) of twenty-three white men from the group of thirty-five patients with Bowen's disease and without evidence of senile keratosis had primary internal cancer. A χ^2 test showed no significant difference in the incidence of primary internal cancer between this group and the 35 white men with senile keratosis and no Bowen's disease.

Similar tests showed greater likelihood of association of primary internal cancer with Bowen's disease than with any of the other disease entities that could be tested. Although the cases of Paget's disease of the breast, xeroderma pigmentosum, and erythroplasia of Queyrat were not suitable for testing, the greater likelihood of association of internal cancer with Bowen's disease is apparent, since there were no primary internal cancers in the last two and only two (5%) in the former.

Review of the Literature

Evidence may be obtained from the reports of others in regard to the development of squamous-cell carcinoma in Bowen's disease and in regard to regional and widespread metastases. In Bowen's[3] patient No. 6 an invasive squamous-cell carcinoma was present in a nodule excised from a large plaque on the chest. There was no evidence of metastasis. In Darier's[2,8] first, third, and fourth patients there was histologic evidence of invasion in their skin lesions and in addition metastasis to the regional lymph nodes. The last patient was followed until death, and at autopsy there was not only malignant infiltration of the regional lymph nodes but also metastasis to the lung and greater curvature of the stomach. The histologic characteristics of the metastasis were similar to those noted in the skin. Other reports regarding invasion, metastasis, or both, in Bowen's disease have been published by Sequeira and Turnbull,[9] Stout,[10] Finnerud and Duncan,[11] and others. There is reliable evidence in the literature regarding the association of other premalignant and malignant lesions of the skin in patients with Bowen's disease. Bowen's[3] patient No. 6, as interpreted and cited by Fraser,[4] had another lesion associated with the Bowen's dermatosis that was histologically a basal-cell carcinoma. Strangely enough, Bowen did not comment on this interesting association, but it is apparent from his description and figures that the basal-cell carcinoma was not a transformation of the Bowen lesion but an unrelated tumor. Sequeira's[9] patient, in addition to precancerous dermatosis, had Bowen's disease with invasive squamous-cell carcinoma and two lesions of typical "rodent ulcer" basal-cell carcinomas. Fraser's[4] patient No. 2 had a lesion of the breast which was similar in clinical appearance to the Bowen's lesions but on microscopic examination proved to be basal-cell carcinoma. Transitional stages could not be found between the lesion of Bowen's disease and the basal-cell carcinoma. Montgomery[12] pointed out the association of Bowen's disease and superficial epithelioma, and his third patient also had typical senile keratosis. It was Montgomery's belief that Bowen's disease occurs independently of superficial epitheliomatosis.

There are few documents in the literature regarding Bowen's disease and internal cancer. Bowen,[13] in 1920, published a brief report on the further course of two cases previously reported. His patient No. 6,

reported first in 1915, died in 1918 of cancer of the pylorus after having had skin lesions for 34 years. There is no indication that Bowen realized the significance of the relationship at that time, other than to support the concept that Bowen's dermatosis was a precancerous lesion. Fraser,[4] in 1928, referred to Bowen's patient No. 6, who, though apparently cured, developed a cancer of the pylorus two years later as a circumstance which was probably not related to the primary disease. In 1953, Jaeger and Delacretaz [14] reported a 71-year-old woman with Bowen's epithelioma of the cheek and Paget's disease of the breast. Mordant,[15] a year later, reported the coexistence of skin metastasis of a renal epithelioma, Bowen's disease, and several pagetoid epitheliomas (superficial epitheliomatosis). Roth,[16] in 1956, diagnosed Bowen's disease from several pieces of skin taken at autopsy. The cause of death was bronchial carcinoma. These latter reports reflect the association of internal cancer in Bowen's disease, although this significance was apparently not realized.

The relation of skin cancer to other malignant lesions has been pointed out by a number of other investigators. Owen,[17] in 1921, reviewed the literature on multiple malignant neoplasms and reported his experiences. Three patients with cancer of the breast also had basal-cell carcinoma of the skin, and in another instance a patient with melanoma of the back had in addition multiple basal-cell carcinomas.

Warren and Gates [18] in a thorough study in 1932 pointed out that a person who had one cancer is definitely more likely to have a second cancer. Conrad and Hill [19] observed that those patients who were working in occupations having a higher rate of cancer of the skin and lip also had cancers at other sites. Stalker, Phillips, and Pemberton,[20] in a study of 54 patients with 97 basal-cell carcinomas, 69 squamous-cell carcinomas, and 1 melanoepithelioma of the skin and lip, noted that 35.4% showed malignant disease in another part of the body. Warren and Gates,[21] in 1940, followed 1,149 persons with basal or epidermoid carcinoma of the skin and observed that 6.7% had cancer of other organs than the skin. In 1944, Warren and Ehrenreich [22] studied 194 patients with multiple primary malignant tumors. Thirteen, or 6.7% of this group, had cancer of the skin and malignant lesions of other organs.

Sommers and McManus,[23] reporting on multiple arsenical cancers of the skin and internal organs, studied 27 patients. Ten (37%) had either pathologic or clinical evidence of internal cancer. In addition, a variety of carcinomas of the skin, including carcinoma in situ (Bowen's disease) occurred. More recently, Roth [16] performed autopsies on 27 vintners from the Rhineland who were exposed to arsenic in the years from 1925 to 1942. Sixteen (59%) of these had internal cancers involving the lung, liver, bile ducts, and esophagus. Five of the twenty-seven had carcinoma of the skin after the onset of hyperkeratosis.

The recognition of Paget's disease of the nipple as an indication of an underlying carcinoma of the breast has long been accepted. Most investigators note that the incidence varies from 85% to 100%. Foote and Stewart [24] state, "We have never had an example where we could say that the underlying ducts were free from involvement." There are no specific statistics in the literature regarding the presence of extramammary Paget's disease and malignant internal lesions, although Pinkus and Gould [25] reported the association in a patient with a mucin-secreting carcinoma of the rectum. He discussed cases of similar involvement reported by Artz and Kren, Eberts, and others. Weiner [26] and others have generally accepted the apocrine-gland origin of Paget's dermatosis. Greeley and Curtin [27] stated, "The disease might be considered a type of primary carcinoma of the apocrine sweat glands that metastasizes into the skin."

No references were found regarding the occurrences of xeroderma pigmentosum with internal cancer. However, it is generally recognized that patients having xeroderma pigmentosum are prone to cancer of the skin and that they tend to die earlier than

would normally be expected. Pillsbury, Shelley, and Kligman [28] list basal-cell carcinoma as the most commonly associated skin cancer but state that occasionally squamous-cell carcinomas and even melanomas and sarcomas spring up in the radiodermatitis-like skin.

Bluefarb,[29] in his textbook on Kaposi's sarcoma, reviewed 360 cases collected in 1951 and earlier. Thirty patients (8.3%) had associated internal malignant lesions. These included six each with Hodgkin's disease and lymphatic leukemia, three each with mycosis fungoides and lymphosarcoma, two each with myeloid leukemia and adenocarcinoma of the colon, and one each with adenocarcinoma of the stomach, hypernephroma, malignant lymphoma, Brill-Symmers disease, osteogenic sarcoma of the tibia, carcinoma of the liver, adenocarcinoma of the cervix, and carcinoma of the prostate. Epstein [30] reviewed published reports on 28 patients with Kaposi's sarcoma and added 7 cases previously unreported. Two (5.7%) of the thirty-five had internal malignant lesions, adenocarcinoma of the rectum, and Hodgkin's disease of the right lung, respectively.

With regard to exfoliative dermatitis, or generalized erythroderma, Ormsby and Montgomery [31] state that the disease "accounts for about a third of all types of cutaneous lymphoblastoma. It is seen especially in the latter decades of life, in which 30% to 50% of all cases of exfoliative dermatitis are of lymphoblastic origin." Pillsbury [28] and his associates pointed out, "Occasionally, the onset of Hodgkin's disease, mycosis fungoides and lymphatic leukemia will be marked by erythroderma and exfoliative dermatitis."

The association of herpes zoster with internal cancer is generally accepted. Blank and Rake [32] stated, "Zoster has been noted following a variety of stimuli or trauma." Among the common ones, he listed cancer of the breast, leukemia, and Hodgkin's disease. He referred to the work of Pendergrass and Kirsh, who noted that 16 (3.9%) of 406 patients with cancer of the breast had herpes zoster. In 12 of the 16 there was evidence of metastasis at the time the zoster appeared. De Moragas and Kierland [33] studied the records of 916 patients with herpes zoster who were seen at the Mayo Clinic between 1935 and 1949. They noted that the most frequently associated diagnosis in these patients (39 cases, or 4.2%) was lymphoma. Pillsbury [28] states that "the most important relation, and one which cannot be doubted, is the occurrence of zoster in relation to malignant disease, including breast cancer, Hodgkin's disease and leukemia."

Of recent interest has been the recognized syndrome of functioning carcinoid. Kierland and Sauer [34] reviewed the cutaneous manifestations and reported six patients studied at the Mayo Clinic. Five of these had shown the characteristic flushing mechanism associated with cyanosis. Shafer, in discussing this paper, referred to the unpublished work of Helwig and Manion, who had collected 261 cases of carcinoid. In six patients (2.3%) the functioning carcinoid syndrome was present.

During the past few years there has been a greater appreciation of the association of dermatomyositis with primary internal cancers. Firmat and Lipsett [35] recently observed four patients with dermatomyositis and cancer, two with carcinoma of the cervix, and one each with carcinoma of the breast and Hodgkin's disease. In this report they referred to the survey of Sheard and Knoepfler.[36,37] In this latter study approximately 600 patients with dermatomyositis were collected from the world literature, and 70 (11.7%) had cancer. Later, Sheard and Knoepfler reported 14 patients of their own with dermatomyositis, and 6 (42.8%) had internal malignant lesions as follows: carcinoma of the breast, 2; carcinoma of the ovary, rectum, colon, and stomach, 1 each. Christianson, Brunsting, and Perry [38] at the Mayo Clinic made a survey of the records of 270 patients with dermatomyositis and noted associated malignant diseases in 6.7% of the cases.

Curth [39,40] for many years has been interested in acanthosis nigricans and has made extensive surveys of this disease. She classified the disease into "benign" and "malignant" types and justified this by the fact that adults suffering from "malignant" acanthosis nigricans pass through puberty without displaying "benign" acanthosis nigricans. Curth [41] states that "in almost 100 per cent of cases of malignant acanthosis nigricans there will be an associated internal adenocarcinoma." The tumors are usually located in the stomach, liver, pancreas, esophagus, gallbladder, intestine, uterus, ovary, mammary gland, and lung. Pillsbury,[28] in his textbook, states: "The remarkable clinical feature of acanthosis nigricans is that 50 per cent of the cases are associated with some fatal form of internal cancer. This is responsible for the subdivision of the disorder into benign and malignant types. The cutaneous manifestations are clinically and histologically identical in both the benign and malignant types."

No statistical review regarding the occurrence of poikiloderma atrophicans vasculare with systemic cancer could be found. Dostrovsky and Sagher [42] reviewed those cases occurring with mycosis fungoides and reported a case of their own. Lever [43] stated, "In rare instances of mycosis fungoides, lesions of poikiloderma atrophicans vasculare develop either as a precursor or as a residuum of plaque-like lesions."

An exhibit by Curth [41] listed several additional non-neoplastic cutaneous lesions associated with malignant internal tumors. No data in regard to incidence were available, but she included the following symptoms and diseases: pruritus, urticaria, acquired ichthyosis, Peutz-Jeghers syndrome, a syndrome of multiple cutaneous and subcutaneous lesions occurring simultaneously with hereditary polyposis and osteomatosis, pachydermoperiostosis, erythema multiforme, erythema gyratum repens, dermatitis herpetiformis, and others. Beerman [44] recently reviewed the literature regarding some aspects of cutaneous cancer. He discussed metastatic cutaneous malignant lesions, the cutaneous manifestations of the lymphoblastomas, cutaneous lesions and internal cancer, and other pertinent associations already mentioned.

Comment

The study of cancer-proneness has long been an avenue of investigation in the attempt to discover etiologic factors inducing malignant growths. In fact, the study of the natural history may be just as important as research in physiopathology, immunochemistry, microbiology, and other complex aspects of cancer. Furthermore, observations on the natural history of a disease in humans may suggest new problems for experimental research that no other approach has to offer. Little is known about the natural history of Bowen's disease. Medical literature contains a number of articles dealing primarily with the possible etiology, but comparatively few authors have been concerned with the subsequent course of patients with Bowen's disease.

Some observations made during the study of our patients merit further discussion. In general, the onset of Bowen's disease is related to age; among 135 patients (35 patients who came to autopsy and 100 who were alive at last report), only one-fifth were less than 35 years of age at the time the lesions were first noticed.

Neither the appearance of the lesions nor the accompanying signs and symptoms of Bowen's disease appeared to be particularly troublesome to the patients. This is supported by the fact that for 23 of the 35 patients studied the interval from onset to removal of the lesion was 5 to 30 years; for 14 of these, the interval ranged from 10 to 30 years.

All 35 patients in this series were Caucasians; however, there were some Negroes, Latin Americans, and Orientals in a supplementary group of more than 100 living patients. No conclusion as to sex distribution can be made because the material from which the patients were drawn was predominantly male.

Bowen's disease usually has certain objective characteristics, but variations in appearance and its similarity to some other cutaneous lesions make clinical diagnosis difficult. An indication of this is seen in the fact that the correct clinical diagnosis was made for only 1 of the 35 patients.

Approximately one-half of the patients had other cutaneous premalignant or malignant lesions, which were either single or multiple. Squamous- and basal-cell carcinoma and senile keratosis were the predominant associated lesions.

Eighty per cent of the patients had either a primary cutaneous tumor with metastasis or had a primary internal cancer. Only squamous-cell carcinoma and a malignant melanoma metastasized from the skin; in two instances the squamous-cell carcinomas arose in Bowen's disease. Biologically, the internal cancers were highly aggressive, since 22 of 24 patients with primary internal cancers had metastatic lesions or generalized spread. When all malignant tumors at all sites are considered, the cancer-proneness of this group becomes even more evident. Thirty-one (89%) of the thirty-five patients had cutaneous or internal cancers in one or more locations. The types and primary sites of the cancers involved all three germ layers, although epithelial structures of the ectoderm and entoderm predominated.

Bowen's disease appeared before the detection of cutaneous premalignant and malignant lesions in 77% of the patients in whom the time intervals were known. Furthermore, it was the first lesion in 93% of the 28 patients with either primary internal cancers or metastasizing cutaneous lesions. Time relationships can be established between the onset of Bowen's disease and the various types of other cutaneous lesions, although some may not be reliable because of their small numbers. Senile keratosis, basal-cell and squamous-cell carcinoma appeared about six years after the onset of Bowen's disease; internal cancer and skin cancers with metastasis, an average of eight and one-half years. The data from Table 5 and Chart 2 suggest that the reticuloendothelial system is the most susceptible and the gastrointestinal tract the most resistant. (The reticuloendothelial system is included in "all other sites" in Chart 2.)

This convincing time relationship between Bowen's disease and other malignant lesions brings up some interesting thoughts. It points to the possibility of a common mechanism for development and perhaps individual predisposition toward cancer. Eight (36%) of twenty-two patients with Bowen's disease had family histories of relatives who had internal cancers. There is a striking similarity in the natural history of patients with Bowen's disease and those who have had prolonged contact or treatment with the inorganic arsenicals. The average latent period of six to eight years from onset of the Bowen's lesion until cutaneous and internal cancers appear is characteristic of the long latent interval of carcinogenic action of arsenic, as reported by Neubauer,[45] Sommers,[23] Roth,[16] and others. Warburg,[46] in his masterly thesis on the origin of cancer cells, made mention of the mysterious latency period and based it on the time in which cellular fermentation increases after a damaging of cellular respiration. He stated, "... when the respiration of body cells has been irreversibly damaged, cancer cells by no means immediately result. For cancer formation there is necessary not only irreversible damaging of the respiration but also an increase in the fermentation. There are a great many remote causes of cancer: tar, rays, arsenic, pressure, urethane; but there is only one common cause into which all other causes of cancer merge, the irreversible injuring of respiration." It might be surmised that whatever the carcinogenic factor present in association with Bowen's disease, its mode of action may well be through irreversible injury to cellular respiration and gradual increase in fermentation, reflected first in epithelial structures of the skin and later in epithelial and reticuloendothelial organs elsewhere in the body. The predominance of involvement of some systems over others might be based upon the roles of these organs in normal body

functions. One fact is established from this study—that cancers associated with Bowen's disease may involve practically all body systems and germ layers.

Certainly, whether Bowen's disease is in itself carcinogenic or is a cutaneous reaction to some carcinogenic agent, it has been clearly shown that people with this disease appear to be susceptible to cancer. In this study, 6 of the 35 patients with Bowen's disease had primary internal cancer which was not detected prior to autopsy. Physicians who remove lesions for which the diagnosis of Bowen's disease is suspected or confirmed should be aware of the need for careful examination and follow-up to ascertain whether malignant lesions, either cutaneous or internal, are also present. It may be that further follow-up of the patients with Bowen's disease who were living at last report may disclose that there are exceptions to cancer-proneness. There is strong evidence from our study that the patient with Bowen's disease is disposed to develop internal cancer. In our series, internal cancer or metastasis from a cutaneous malignant tumor caused the deaths of 28 patients, 21 of them within five years after surgical biopsy or removal of the first lesion of Bowen's disease. It cannot be said that most of the seven patients who died of other causes would not have developed internal or metastasizing skin cancers eventually, since five of the seven died within three years after removal of the Bowen's lesion.

Evaluation of treatment may not be considered complete because of the short follow-up period, although some conclusions can be drawn. The lesions seem fairly resistant to x-ray and prone to recur after desiccation and curettement. Two lesions treated with radium were apparently cured; the reason for this, especially since similar lesions failed to respond to x-ray, cannot be explained. Adequate surgical excision seems to be the treatment of choice whenever possible. The necessity for adequate removal is indicated by the fact that the lesions of Bowen's disease in four patients showed invasion as squamous-cell carcinoma and that two developed widespread metastasis.

Controls and Comparative Studies

In Table 6 the per cent of associated primary internal cancers in the 35 patients with Bowen's disease was compared successively with that in squamous-cell carcinoma of the skin, senile keratosis, and exfoliative dermatitis. There was no instance of Bowen's disease in any of the latter groups.

The χ^2 tests indicated that the difference between Bowen's disease and senile keratosis in relation to primary internal malignant lesions was not statistically significant at the 5% level of probability. However, patients with Bowen's disease were more likely to have primary internal cancer than were patients with squamous-cell carcinoma of the skin. The odds were 49 to 1 against the probability of finding, by random sampling, values of χ^2 greater than the value found in this series.

Statistically, the odds are greater than 1,999 to 1 that in samples such as these, primary internal cancers are more likely to be associated with Bowen's disease than with exfoliative dermatitis. Three of the patients with exfoliative dermatitis and four of those with Bowen's disease had lymphomas. A χ^2 test with Yates' correction indicated no significant difference between the two diseases with respect to presence of lymphomas.

Certain important features became apparent in the study of the comparative and the control groups (Tables 6 and 7). We were surprised to find that patients who have senile keratosis are also prone to have primary internal cancer and cannot be statistically separated from Bowen's disease regarding this association. Even though Bowen's disease and senile keratosis have different clinical and histological features, they act biologically in the same fashion.

Cutaneous squamous-cell carcinoma, on the contrary, has a significantly lower incidence of associated primary internal malignant tumors and of itself may act as the aggressive primary carcinoma. As a group,

though, people who have squamous-cell carcinoma of the skin cannot be statistically separated from Bowen's disease in regard to biological results, i. e., death either from widespread metastases from cutaneous squamous-cell carcinoma or from an internal cancer or both.

The generally accepted view is that a high incidence of internal cancer, particularly the lymphomas, occurs in association with exfoliative dermatitis. The incidence was surprisingly low in our series. Even though lymphoma was the predominant associated cancer in our group of patients with exfoliative dermatitis, the number of cases was not significantly different from the number found in association with Bowen's disease.

Many observers have classified erythroplasia of Queyrat as Bowen's disease of the glans penis because of the striking microscopic resemblance to Bowen's disease of the skin. The natural history of our patients suggests that erythroplasia of Queyrat is a different disease from Bowen's disease of the skin. In our material, there is apparently no association of erythroplasia of Queyrat with internal cancer and there is an absence of cutaneous lesions of Bowen's disease and premalignant and malignant lesions of the skin.

Our group of patients with arsenical keratosis was small, but the indication is that the association with internal and cutaneous cancer is certainly no greater than with Bowen's disease. The recent reports of others support this impression. The microscopic features of arsenical keratosis and Bowen's disease of the skin may be practically identical. However, in our patients with Bowen's disease, there was no history of ingestion of arsenic.

Of interest was the presence of herpes zoster in three patients with Bowen's disease and internal cancer. Two of these had malignant neoplasms located in the genitourinary tract, and some of the patients from the comparative study on herpes zoster had their internal malignant tumors located in the lung, thyroid, pancreas, and bone. This might indicate that physicians should suspect, to a greater degree, other sites of origin of internal cancer in addition to the lymphomas and breast carcinoma in older debilitated patients with herpes zoster.

Because of our observations regarding senile keratosis, cutaneous squamous-cell carcinoma, and erythroplasia of Queyrat, we plan to study much larger groups of patients with these lesions and report on each in detail.

Finally, we wish to alert physicians who care for patients with Bowen's disease of the skin to the association of cutaneous and internal cancer, particularly in persons in the fifth and sixth decades of life. Early detection and treatment might well lengthen the life expectancy of this apparently cancer-prone group.

Summary and Conclusions

The association of Bowen's disease of the skin with internal and cutaneous cancer is reported. Thirty-five patients with Bowen's disease, who either came to autopsy or who died after surgical pathological examination of internal organs, were studied. Anatomically, the lesions were single or multiple and occurred on both exposed and unexposed areas of the body. Clinically, the lesions appeared as lenticular polycyclic, erythematous, pigmented, crusty, scaly, keratotic, nodular, and ulcerated plaques; they were sharply demarcated from the surrounding tissue. The clinical diagnosis was most frequently some variety of carcinoma. The disease involved predominantly the older age groups, and in this series the average duration from onset to removal was 7.8 years. The lesions in this group of 35 occurred only in white patients, but the supplementary group included Negro, Oriental, and Latin American patients.

Twenty-eight (80%) of the 35 patients were observed to have one or more primary internal cancers, or a primary cancer of the skin with metastasis, at an average of 8.5 years after onset of Bowen's disease. Twenty-six of these twenty-eight patients had metastatic lesions or generalized spread

from their primary tumors. Furthermore, 15 of the group of 35 patients had a total of 49 premalignant and malignant cancers of the skin that appeared on an average of 6.2 years later than their Bowen's disease. Cancer-proneness of the entire group is even more evident when it is considered that 31 (89%) of the patients had primary cancer in one or more locations. All three germ layers were involved, and the sites, in order of frequency, were the respiratory system, gastrointestinal tract, genitourinary organs, reticuloendothelial system, skin, breast, and endocrine system (Table 5). Three of the group with internal malignant tumors also had herpes zoster during their terminal illness.

Excision of the Bowen lesion was the treatment of choice, for the process tended to recur or not to respond to x-ray therapy, desiccation, and curettement. Two lesions were apparently cured with radium.

The average follow-up period for the 35 patients from the time Bowen's disease was first diagnosed until death was 3.4 years. Thus, there was a poor prognosis once internal or metastasizing cutaneous cancer occurred. The short follow-up period in many of our patients was due to death from internal cancer. Hereditary or some other common predisposition to the development of cancer was suggested by the occurrence of internal cancer in one or more members in 8 (36%) of 22 families. Arsenic could not be implicated as an etiological agent in Bowen's disease.

In 4 of the 35 patients, the Bowen's lesions invaded the corium as squamous-cell carcinoma; in 2 of the 4 there was metastasis to internal organs. The microscopic picture in Bowen's disease resembles the changes in arsenical keratosis and erythroplasia of Queyrat. Patients with Bowen's disease were statistically similar to those with senile keratosis in regard to the prevalence of associated primary internal cancer. In contrast, patients with primary cutaneous squamous-cell carcinoma had a much lower incidence of internal cancer than did those who had Bowen's disease. Primary internal cancer was much less frequent in patients with exfoliative dermatitis than with Bowen's disease, but the prevalence of lymphomas was approximately equal in the two groups.

The association of Bowen's disease of the skin with internal and cutaneous cancer may well represent a cutaneous manifestation of a systemic carcinogenic disease process.

Armed Forces Institute of Pathology, 6825 16th St., N. W.

REFERENCES

1. Bowen, J. T.: Precancerous Dermatoses: A Study of 2 Cases of Chronic Atypical Epithelial Proliferation, J. Cut. Dis. 30:241-255 (May) 1912.

2. Darier, J.: La Dermatose précancéreuse de Bowen, dyskératose lenticulaire et en disques, Ann. dermat. et syph. 5:449-471, 1914.

3. Bowen, J. T.: Precancerous Dermatoses: A Sixth Case of a Type Recently Described, J. Cut. Dis. 33:787-802 (Dec.) 1915.

4. Fraser, J. F.: Bowen's Disease and Paget's Disease of the Nipple, Arch. Dermat. & Syph. 18:809-828 (Dec.) 1928.

5. Neubecker, R. D.: Personal communication to the authors, July, 1958.

6. Cox, F. H., and Helwig, E. B.: Kaposi's Sarcoma, Cancer 12:289-298 (March-April) 1959.

7. Manion, W. C., and Helwig, E. B.: Malignant Carcinoid, to be published.

8. Darier, J.: Le Cancer de la dermatose précancéreuse de Bowen, Ann. dermat. et syph. 1:49-61, 1920.

9. Sequeira, J. H., and Turnbull, H.: Multiple Carcinoma of the Skin: Precancerous Dermatosis of Bowen, Brit. J. Dermat. 33:173-181, 211-227 (May-June) 1921.

10. Stout, A. P.: Malignant Manifestations of Bowen's Disease, New York J. Med. 39:801-809 (April) 1939.

11. Finnerud, C. W., and Duncan, E. T.: Bowen's Precancerous Dermatosis ("Bowen's Disease"), M. Clin. North America 33:125-134 (Jan.) 1949.

12. Montgomery, H.: Superficial Epitheliomatosis, Arch. Dermat. & Syph. 20:339-357 (Sept.) 1929.

13. Bowen, J. T.: Precancerous Dermatosis: The Further Course of 2 Cases Previously Reported, Arch. Dermat. & Syph. 1:23-24 (Jan.) 1920.

14. Jaeger, H., and Delacretaz, J.: Epithelioma de Bowen de la joue et maladie de Paget du sein, Dermatologica 107:256-257, 1953.

15. Mordant, H.: Coexistence dans la même région d'épithéliomas pagétoides, de maladie de

Bowen, et d'une métastase cutanée d'un carcinome viscéral, Arch. belges dermat. et syph. 10:229-231 (July) 1954.

16. Roth, F.: The Sequelae of Chronic Arsenic Poisoning in Moselle Vintners, German M. Month. 2:172-175 (June) 1957.

17. Owen, L. J.: Multiple Malignant Neoplasms, J. A. M. A. 76:1329-1333 (May 14) 1921.

18. Warren, S., and Gates, O.: Multiple Primary Malignant Tumors: A Survey of the Literature and a Statistical Study, Am. J. Cancer 16: 1358-1414 (Nov.) 1932.

19. Conrad, K. K., and Hill, A. B.: Mortality from Cancer of the Skin in Relation to Mortality from Cancer of Other Sites, Am. J. Cancer 36: 83-97 (May) 1939.

20. Stalker, L. K.; Phillips, R. B., and Pemberton, J. de J.: Multiple Primary Malignant Lesions, Surg. Gynec. & Obst. 68:595-602 (March) 1939.

21. Warren, S., and Gates, O.: Cancer of the Skin in Relation to Multiple Malignant Growths, J. A. M. A. 115:1705-1707 (Nov. 16) 1940.

22. Warren, S., and Ehrenreich, T.: Multiple Primary Malignant Tumors and Susceptibility to Cancer, Cancer Res. 4:554-570 (Sept.) 1944.

23. Sommers, S. C., and McManus, R. G.: Multiple Arsenical Cancers of Skin and Internal Organs, Cancer 6:347-359 (March) 1953.

24. Foote, F. W., Jr., and Stewart, F. W.: A Histologic Classification of Carcinoma of the Breast, Surgery 19:74-99 (Jan.) 1946.

25. Pinkus, H., and Gould, S. E.: Extramammary Paget's Disease and Intraepidermal Carcinoma, Arch. Dermat. & Syph. 39:479-502 (March) 1939.

26. Weiner, H. A.: Paget's Disease of the Skin and Its Relation to Carcinoma of the Apocrine Sweat Glands, Am. J. Cancer 31:373-403 (Nov.) 1937.

27. Greeley, P. W., and Curtin, J. W.: Extramammary Paget's Disease of the Skin, J. A. M. A. 155:1054-1055 (July 17) 1954.

28. Pillsbury, D. M.; Shelley, W. B., and Kligman, A. M.: Dermatology, Philadelphia, W. B. Saunders Company, 1956.

29. Bluefarb, S. M.: Kaposi's Sarcoma, Springfield, Ill., Charles C Thomas, Publisher, 1957.

30. Epstein, E.: Extracutaneous Manifestations of Kaposi's Sarcoma: A Systemic Lymphoblastoma, California Med. 87:98-103 (Aug.) 1957.

31. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, Ed. 8, Philadelphia, Lea & Febiger, 1954.

32. Blank, H., and Rake, G.: Viral and Rickettsial Diseases of the Skin, Eye and Mucous Membranes of Man, Ed. 1, Boston, Little, Brown & Company, 1955.

33. de Moragas, J. M., and Kierland, R. R.: Outcome of Patients with Herpes Zoster, A. M. A. Arch. Dermat. 75:193-196 (Feb.) 1957.

34. Kierland, R. R.; Sauer, W. G., and Dearing, W. H.: The Cutaneous Manifestations of the Functioning Carcinoid, A. M. A. Arch. Dermat. 77:86-88 (Jan.) 1958.

35. Firmat, F. J., and Lipsett, M. B.: Cancer and Dermatomyositis, Cancer 2:63-66 (Jan.-Feb.) 1958.

36. Sheard, C., Jr., and Knoepfler, P. T.: Dermatomyositis and the Incidence of Associated Malignancy, Connecticut M. J. 20:626-630 (Aug.) 1956.

37. Sheard, C., Jr., and Knoepfler, P. T.: Dermatomyositis and the Incidence of Associated Malignancy, A. M. A. Arch. Dermat. 75:224-227 (Feb.) 1957.

38. Christianson, H. B.; Brunsting, L. A., and Perry, H. O.: Dermatomyositis: Unusual Features, Complications, and Treatment, A. M. A. Arch. Dermat. 74:581-589 (Dec.) 1956.

39. Curth, H. O.: Significance of Acanthosis Nigricans, A. M. A. Arch. Dermat. & Syph. 66: 80-100 (July) 1952.

40. Curth, H. O.: Acanthosis Nigricans and Its Association with Cancer, Arch. Dermat. & Syph. 57:158-170 (Feb.) 1948.

41. Curth, H. O.: Dermatoses and Malignant Internal Tumors, A. M. A. Arch. Dermat. 71:95-107 (Jan.) 1955.

42. Dostrovsky, A., and Sagher, F.: Poikiloderma as the Initial Stage of Mycosis Fungoides, Arch. Dermat. & Syph. 51:182-188 (March) 1945.

43. Lever, W. F.: Histopathology of the Skin, Ed. 2, Philadelphia, J. B. Lippincott Company, 1954.

44. Beerman, H.: Some Aspects of Cutaneous Malignancy, Am. J. M. Sc. 233:456-472 (April) 1957.

45. Neubauer, O.: Arsenical Cancer: A Review, Brit. J. Cancer 1:192-251 (June) 1947.

46. Warburg, O.: On the Origin of Cancer Cells, Science 123:309-314 (Feb.) 1956.

Epidermal Changes Associated with Sclerosing Hemangiomas

HILLARD J. HALPRYN, M.D., and ARTHUR C. ALLEN, M.D., Miami, Fla.

As a rule, dermal neoplasms are associated either with no alteration of the overlying epidermis or with simple atrophy, the latter as if by pressure from the dermal mass. However, there are several dermal tumors which characteristically and contrarywise provoke epithelial activity. The most familiar of these is the so-called granular-cell myoblastoma, which is usually characterized by an associated pseudoepitheliomatous hyperplasia, so striking as to be mistaken occasionally for a squamous-cell carcinoma. The pathogenesis of this reaction has so far eluded clarification.

Not generally appreciated is the fact that the sclerosing hemangioma (dermatofibroma lenticulare, histiocytoma, nodular subepidermal fibrosis) is also frequently overlaid by evidence of epidermal activity which takes a variety of morphologic forms, including neoplasia.

Because of the dearth of information concerning both the existence and nature of the phenomenon embodying the concomitance of epidermal and dermal lesions, the following systematic study was undertaken.

Methods and Materials

All lesions diagnosed pathologically as dermatofibroma, histiocytoma, nodular subepidermal fibrosis or sclerosing hemangioma in the three-year period from March, 1955, to March, 1958, were reexamined with particular attention given to any epidermal changes overlying the tumor. A total of 130 lesions from 116 patients were examined. However, it was found, on reviewing the slides, that 16 lesions (from 14 patients) were scars or other fibrous tumors that did not fit into any of the above diagnostic categories. These were, therefore, eliminated from the total series. Of the remaining 114 lesions (from 102 patients), 77 were from women and 37 from men.

The age of the patients ranged from 17 to 72 years, with approximately 85% of the cases included in the 41- to 60-year-old age group; 58% of all lesions occurred on the lower extremities; 14%, on the upper extermities; 10%, on the chest; 8%, on the back; and 2%, on the face. This is in general agreement with the usually stated distribution of these lesions.

The indication for biopsy was not specified in most cases, and preoperative clinical diagnoses were available in only 50 (44%) of the 114 lesions reviewed. In most cases designations such as "lesion," "growth," "nevus," or "cyst" were used. In no instance did the submitting physician use the term "dermatofibroma" or one of its synonyms; and in no case was any notation made about surface changes above the lesion.

Results

Some degree of acanthosis was found in 80 (70%) of the lesions examined, while in 6 cases (5%) there was mild atrophy of the epidermis overlying the lesions. Aside from these minor changes, significant epidermal changes were found in 29 (25%) of the 114 specimens reviewed. It is of interest to note that in only one instance, that of a basal-cell carcinoma, did the pathologist who wrote the original report mention any of the abnormal surface changes.

The significant changes noted were of three general types.

1. *Basal-Cell Carcinoma.*—Basal-cell carcinomas were found in nine cases (or 8% of all lesions examined). Two of these were of the intraepidermal type; the others showed more advanced growth (Figs. 1-5).

2. *Seborrheic Keratosis.*—Several vari-

Submitted for publication Dec. 10, 1958.

From the Department of Pathology (Dr. Allen) and the Division of Dermatology (Dr. Halpryn), University of Miami School of Medicine, Jackson Memorial Hospital.

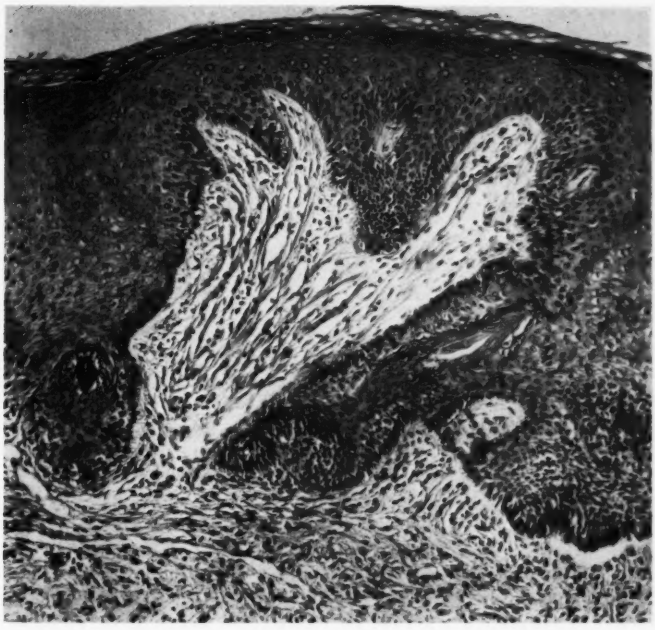


Fig. 1.—Acanthosis and intra-epidermal basal-cell epithelioma overlying a sclerosing hemangioma; × 108.

eties of seborrheic keratosis were seen in 13 cases (or 11% of all lesions studied) (Fig. 6).

3. *Keratoacanthosis.*—In seven cases (or 6% of all lesions examined) a combination of hyperkeratosis, acanthosis, and papillomatosis produced a microscopic picture of a keratoacanthotic lesion very similar to the so-called hard nevus of Unna. This change we have designated keratoacanthosis (Figs. 7 and 8).

The relationship between the age of the patients and the type of abnormal epidermal change is shown in Table 1.

From this we see that although 77% of the basal-cell carcinomas occurred in the 41- to 60-year age group, the younger age group (17 to 40 years) accounted for 71%

Fig. 2.—Acanthosis with intra-epidermal basal-cell carcinoma overlying a sclerosing hemangioma; × 80.

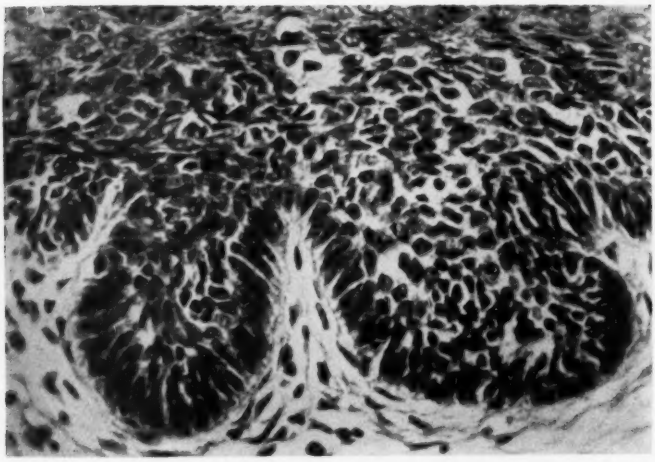


Fig. 3.—High power of field from Figure 2, illustrating the neoplastic nests of basal cells; × 240.

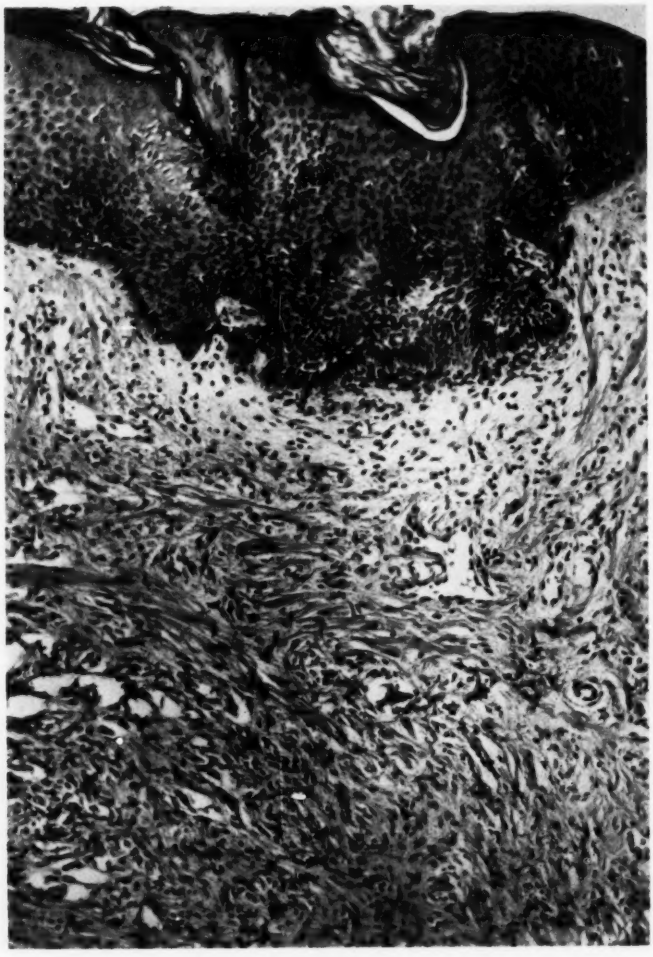


Fig. 4.—Intra-epidermal basal-cell epithelioma overlying a sclerosing hemangioma; × 80.

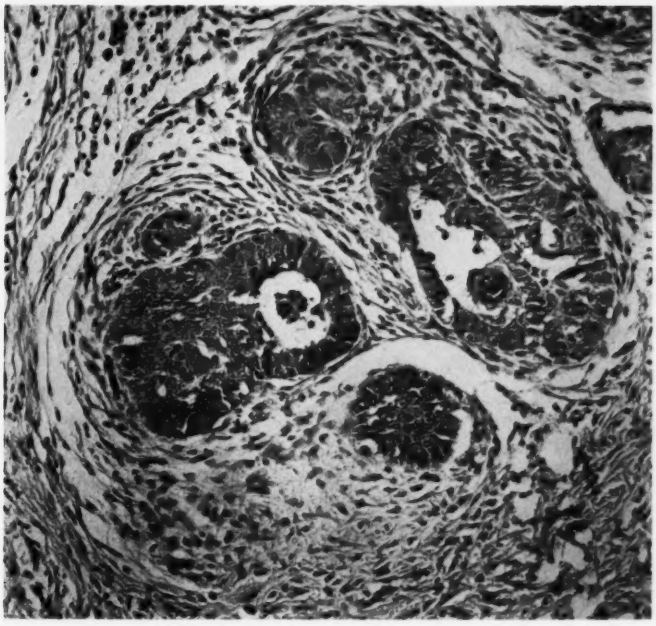


Fig. 5.—Infiltrating basal-cell epithelioma overlying a sclerosing hemangioma.

of the keratoacanthotic lesions and 7% of the seborrheic keratoses. Thus, the younger age groups, while constituting only 15% of the total series, showed a disproportionately high incidence of seborrheic keratoses and keratoacanthosis.

The relationship between the type of surface abnormality, the location of the tumor, and the sex of the patient was also studied (Table 2).

Analysis of this material, adjusted for the preponderance of females in the over-all series, showed that seborrheic keratosis and keratoacanthosis occurred with equal frequency in males and females. However, in the case of basal-cell carcinoma, eight of the nine lesions were in females, on the leg.

The possibility that these epidermal changes might be a response to the stimulation from a mass below the surface was

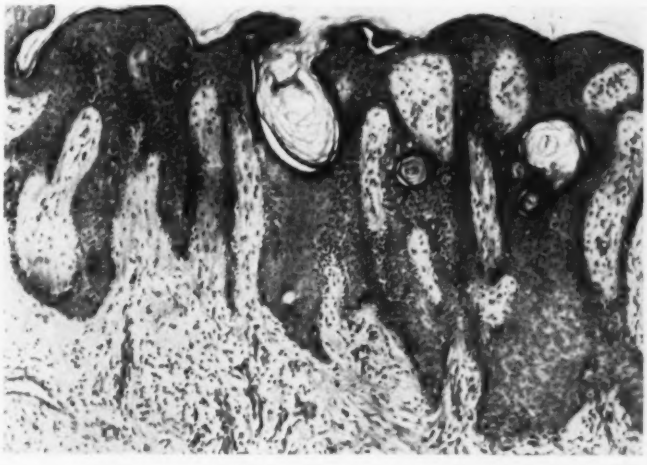
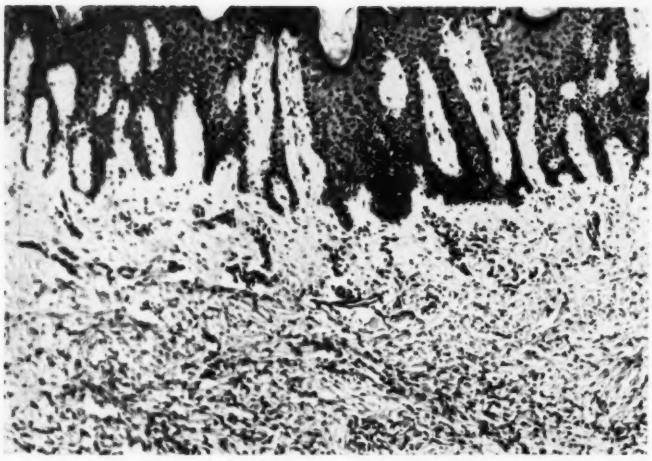


Fig. 6.—Seborrheic keratosis overlying a sclerosing hemangioma, × 80.



7.—Simple acanthosis in association with a sclerosing hemangioma; × 80.

investigated by examining a series of benign cysts, scars, keloids, and other fibrous tumors to see if the presence of any tumor mass would induce similar epidermal changes. No similar epidermal changes were found in any such lesions reviewed.

The distance of the tumor from the epidermis was also measured to see if the epidermal changes could be the result of a trophic disturbance. Here again no relationship was found between the depth of the tumor and the presence of significant overlying epidermal changes.

The relationship between the duration of the tumor and the presence of the surface change could not be studied because of inadequate data.

Comment

The limitations of a study such as this are obvious. The lesions studied were those submitted to a large hospital pathology laboratory. None of these lesions was submitted by a dermatologist or by the dermatology service. It is reasonable to assume that most lesions of this kind are not

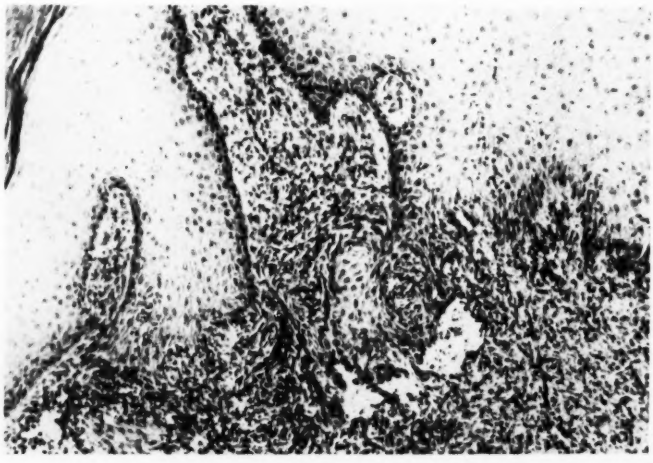


Fig. 8.—Pseudoepitheliomatous hyperplasia overlying a sclerosing hemangioma; × 400.

TABLE 1.—*Relationship Between Age of Patients and Type of Epidermal Change*

Age Group	Basal-Cell Carcinoma	Keratoacanthosis	Seborrheic Keratosis
10-20	1	1	1
21-30	0	3	3
31-40	1	1	6
41-50	3	1	1
51-60	4	1	2

biopsied. From the available data we do not know why these particular lesions were selected for biopsy. Probably many of them were removed for cosmetic reasons, or because they were causing irritation or itching. However, we must not lose sight of the fact that the series might be weighted by having these particular lesions removed because of a suspicious surface change. All we can say is that if this were the case, no mention of this was ever made by the submitting surgeon.

The presence of hyperkeratotic and acanthotic changes in the epidermis overlying these tumors is noted in many of the standard textbooks of dermatology and dermatohistopathology. However, in only one such text is the concomitant presence of sclerosing hemangiomas with basal-cell carcinomas and seborrheic keratoses mentioned.[1]

The only relevant previous report was that of Biberstein, in 1933,[2] who described a group of fibromas with atypical epithelial proliferations found only on the extremities in women. The proliferations resembled intraepidermal basal-cell carcinoma and were characterized by having a distinct gap below the epidermal off-shoots. In our series all the basal-cell carcinomas occurred over lesions on the lower extremities in women, with the exception of one which occurred in a male. This latter lesion was on the abdomen. Although only two of our basal-cell carcinomas resembled the type of lesion depicted by Biberstein, it is possible that the differences are only in the stage of development.

Summary

One hundred fourteen lesions diagnosed as dermatofibroma, histiocytoma, nodular subepidermal fibrosis, and sclerosing hemangioma by a large hospital laboratory were restudied, looking for changes in the epidermis overlying the tumor.

Twenty-five per cent of these lesions had significant epidermal changes. Keratoacanthotic lesions similar in histology to the hard nevus of Unna were found in six per cent of cases. Seborrheic keratoses were found in 11% of cases and basal cell carcinomas were found in 8% of cases.

All of the basal-cell carcinomas overlay lesions of the lower extremities of women. The keratoacanthotic lesions and the seborrheic keratoses occurred most commonly in patients in a younger age group (under 40).

No correlation could be made between the distance of the lesion from the surface and the abnormal epidermal changes.

Similar epidermal changes were not found

TABLE 2.—*Relationship Between Type of Surface Abnormality, Location of Tumor, and Sex of Patient*

	Total Lesions at This Site	Total Abnormal Epidermal Changes at This Site	Basal-Cell Carcinoma		Keratoacanthosis		Seborrheic Keratosis	
			F	M	F	M	F	M
Upper extremity	17	1	0	0	0	1	0	0
Lower extremity	66	19	8	0	5	0	4	2
Chest	11	0	0	0	1	0	3	0
Abdomen	9	3	0	1	0	0	1	1
Back	9	2	0	0	0	0	0	2

in a series of other fibrous tumors and benign cysts.

Conclusions

Significant epidermal changes were found in association with sclerosing hemangioma (dermatofibroma) in 25% of cases.

Such changes are not apt to be seen or noted by the pathologist unless specifically looked for.

A causal relationship between the dermal and epidermal changes was suspected but no one factor could be incriminated.

University of Miami School of Medicine, Jackson Memorial Hospital (36).

REFERENCES

1. Allen, A. C.: The Skin: A Clinicopathologic Treatise, St. Louis, The C. V. Mosby Company, 1954.

2. Biberstein, H.: Fibrome mit atypischer Epithelwucherung, Arch. Derm. u. Syph. 164:69, 1931,

Monoporous and Polyporous Acne

JOHN B. WATSON, M.D., Hollywood, Calif.

A comedo, or blackhead, may be defined as a plug of sebaceous material found in a duct of a sebaceous gland. It is most commonly seen as the elementary lesion of acne vulgaris, but it may also be present in linear nevi, postradiation atrophy, hidradenitis suppurativa, and tar acne.[1-3]

A single comedo may have more than one opening on the skin. The term "double comedo" (Ormsby, as quoted by Ormsby and Montgomery[4]) was used to describe a comedo having two openings which were connected beneath the skin (Fig. 1*b*). No name was given to the comedo which had more than two openings on the skin.

The term "grouped comedones" (Fig. 1*c*) is used to describe a patch of numerous blackheads, each of which has a single opening on the skin (Thin, as quoted by Ormsby and Montgomery).

A giant comedo (Fig. 1*g*) describes any huge blackhead which has one or more openings on the skin and which contains an unusually large mass of sebaceous material.

In order to describe how many openings any single comedo may have, the adjectives "monoporous" (one opening), "diporous" (two openings), "triporous" (three openings), and "polyporous" (many openings) are proposed. The "porous" suffix is derived from the Greek word "poros," meaning pore or passage. The prefixes are accordingly derived from Greek also.

A monoporous comedo is to be distinguished mainly from a polyporous comedo. The former is a comedo with only one opening on the skin (Fig. 1*a*). The latter includes any comedo with more than one opening on the skin (Fig. 1*b*, *c*, *d*, and *g*).

A practical test for determining the presence of a diporous comedo is to pass a small hypodermic needle through two adjacent connecting openings. Figure 2 shows two needles in a triporous comedo. Simple inspection, without probing, is usually sufficient to detect the presence of polyporous comedones.

Monoporous comedones are often unaccompanied by polyporous comedones.

When polyporous comedones are present, monoporous comedones are usually present too.

Submitted for publication Nov. 13, 1958.

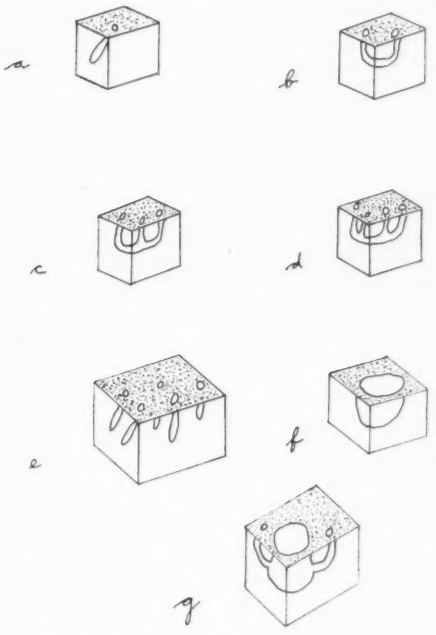


Fig. 1.—Schematic drawings of various comedonal situations. (*a*) Monoporous comedo. (*b*) Diporous comedo ("double comedo"). (*c*) Triporous comedo. (*d*) Polyporous comedo. (*e*) Grouped comedones (monoporous). (*f*) Acne scar formed from a triporous comedo. The epithelial bridges have been destroyed, causing the three pores to coalesce and to form one large pitted scar. (*g*) Giant comedo, formed from a polyporous comedo.

Fig. 2.—Triporous comedo on the nuchal area, with two hypodermic needles piercing its three orifices.

In designating the correct morphologic diagnosis for a particular acne patient, the terms monoporous or polyporous could be combined with other morphological adjectives, such as pustular, excoriated, papular, seborrheic, cystic, and keloidal. Examples might be seborrheic monoporous acne, cystic polyporous acne, excoriated papular monoporous acne, and pustular cystic polyporous acne. Such diagnostic labels would help to explain the condition of each acne patient to both layman and physician. The indefinite diagnosis of acne vulgaris (common acne) fails to intimate the severity, course, treatment, or sequelae of the disease.

These proposed morphologic terms are of importance mainly in determining the prognosis and treatment of acne. When only monoporous comedones are present in acne, the disease is usually mild, superficial, short in duration, nonscarring, and responsive to treatment. If polyporous comedones are also present, the acne is usually severe, deep, chronic, recurrent, familial, scarring, and often resistant to treatment (Table).

The pathogenesis of acne scarring includes the pyogenic infection of the polyporous comedo, with subsequent inflammatory destruction of the epithelial bridges separating the two or more comedonal orifices (Fig. 1*f*). This inflammatory marsupialization allows a natural debridement of the comedo. The end-result is pitted scarring, also described as crateriform or ice-pick scars. These scars have typical shapes, depending upon how many pores the comedo had as well as the extent to which the epithelial bridges are destroyed (Figs. 3 and 4).

The simplest treatment of all comedones, regardless of type, is gentle expression with a comedo extractor. When the comedonal contents are small, as in the average monoporous comedo of mild monoporous acne, the need for mechanical removal is not as important as when the comedonal contents are large, as in polyporous comedones of severe polyporous acne. All comedonal

Comparison of Monoporous Acne and Polyporous Acne

	Monoporous Acne	Polyporous Acne
Essential morphology	Single opening comedones only (Fig. 1 *a*)	Both single- & multiple-opening comedones (Fig. 1)
Additional morphology	May be none; few papules & pustules are common	Papules, pustules, abscesses, cysts, acne scarring, giant comedones (Fig. 1*g*)
Location in dermis	Superficial	Superficial & deep
Familial history	Occasionally	Usually
Severity	Usually mild	Usually severe
Duration of disease	Months	Years
Complications	Usually none; may become pustular	Pustules, abscesses, cellulitis, pyodermas
Spontaneous remission	Usually early, in the teens	Usually late; in the 20's or beyond
Response to treatment	Usually good results with minimal therapy	Usually poor results with maximal therapy
Sequelae	None	Acne scarring, sebaceous cysts, keloids, steatocystoma multiplex
Need for dermabrasion	None	Occasionally

cavities tend to shrink temporarily after the comedo is removed. Even though the cavity usually refills with another comedo, the subsequent comedones are often smaller than the preceding ones.

It may be that the potential cavities of polyporous comedones never disappear. However, they may shrink to such a small size as to be clinically insignificant. It would be logical to assume that treatments which would shrink the comedonal cavities should cure the acne without subsequent scar formation.

Nature's remedy for shrinking comedonal spaces is the aging process. As acne patients grow out of their teens and 20's, the number of comedones naturally decreases.

The most effective known artificial agent for shrinking comedonal spaces is an adequate course of x-ray therapy early in the course of the disease, before acne scarring has occurred. Radiation atrophy of many comedonal spaces occurs before obvious clinical atrophy of the rest of the skin is seen. A small amount of x-ray therapy, e. g., one dose of 75 r, may improve acne temporarily by its beneficial effect on inflammation. However, a large amount of x-ray therapy, e. g., 9 to 12 or more weekly doses of 75 r each, is necessary to shrink comedonal spaces.

Fig. 4.—Closer view of the same patient with polyporous acne. Crateriform scars and polyporous comedones are demonstrated.

Fig. 3.—Severe pitted scarring in polyporous acne. Three obvious polyporous comedones are encircled.

Treatment of polyporous comedones should not be that of incising the epithelial bridges between the pores, since a crateriform scar results. On areas where the cosmetic result may not be important, such as the buttocks of men, surgical marsupialization of the polyporous comedo could be done. Marsupialization eliminates polyporous comedones, but on exposed areas the resultant scarring is more objectionable than the disease.

In relation to polyporous comedones, dermabrasion is another method of marsupialization. Its advantage over scalpel marsupialization is its leveling action on

the noticeable edges of the comedonal crater. Superficial dermabrasion in an area of polyporous comedones may result in unroofing comedonal cavities and thus cause new crateriform scars. The remedy for this occurrence could be further dermabrasion, unless the comedonal cavities extended too deeply in the dermis to be safely treated with this modality.

Summary

The diagnostic phrases of monoporous acne and polyporous acne are suggested. Monoporous acne has blackheads which have only one opening on the skin. Polyporous acne has blackheads with two or more openings on the skin as well as monoporous blackheads.

The use of these contrasting diagnoses will aid in the prognosis and treatment of acne patients.

6253 Hollywood Blvd. (28).

REFERENCES

1. Carney, R. G.: Linear Unilateral Basal-Cell Nevus with Comedones: Report of a Case, A. M. A. Arch. Dermat. & Syph. 65:471-476, 1952.

2. Hartman, M. S.: Postradiation Comedos, Arch. Dermat. & Syph. 62:440-441, 1950.

3. Allington, H. V.: Anal Comedos and Pruritus Ani, Arch. Dermat. & Syph. 59:490, 1949.

4. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, Philadelphia, Lea & Febiger. 1943.

The History of Dermatology as Depicted on Postage Stamps

SAMUEL M. BLUEFARB, M.D., Chicago

I should like to discuss a somewhat different phase of the history of dermatology, namely, philatelic dermatology. Although I am aware that history is of interest only to those who have reached the "metal" age (i. e., gold in the teeth, silver in the hair, and lead in the pants), it is considered to be a fascinating avocation for physicians who have reached senility, an interesting "side line" for antiquarians, and a hobby for the sentimentalist. As you know, a sentimentalist is an overly emotional person to whom tears come easily. This increase of fluid is not limited to the eyes, however, since other organs, such as the bladder, may be similarily affected. Therefore, I will be most understanding if any sentimentalists find it necessary to leave the room. Because I have not quite reached this "metal" or the "sentimental" stage, my interest in the history of dermatology has only been stimulated by a philatelic avocation.

In many countries there is an awareness that many physicians, research scientists, medical discoveries, and medical institutions are equally as important as their elected leaders, dictators, or political accomplishments. This fact has led to an increasing interest in philately as a means of recognizing and honoring the citizens or institutions contributing to the advancement of medicine.

I am sure any philatelist will agree that a study of "medical" stamps will prove that the history of medicine is a most interesting avocation and also that we all eventually hope to be "amateur historians."

Submitted for publication Jan. 26, 1959.

Presidential Address Read at the Annual Meeting of the Chicago Dermatological Society, Jan. 21, 1959.

From the Department of Dermatology, Northwestern University Medical School, and Cook County Hospital.

Philately

Early History.—The first document pertaining to the history of medicine is the Egyptian "Papyrus Ebers," which was recorded only 4,000 years ago. The most ancient medical figure portrayed on a postage stamp is "Thoth the Wise," the "ibis-headed moon god," whose name means "logos," or "the word." He was reputed to be the author of the Ebers Papyrus and was the god of healing who considered the ibis and cynocephalic baboon to be sacred. In 1925 three postage stamps were issued in Egypt to commemorate the Geographical Congress. Of these, one showing Thoth carving the name of King Fuad is illustrated (No. 106) (Fig. 1). Primitive man believed that disease was due to "evil spirits," and the first physicians were medicine men or magicians who endeavored to expel the demons of diseases by incantations, charms, or magical rites.

A stamp (No. 155) issued by the Belgian Congo in 1931 shows a medicine man or witch doctor. A recent stamp, issued by Papua and New Guinea, also depicts a medicine man (No. 139).

The practice of tattooing is undoubtedly of very ancient prehistoric origin. The most extensive tattooing was done by the Laos of Indochina, who covered large areas of the body with fantastic figures of animals. The Maori's of New Zealand concentrated on tattooing the face (No. 167). The Chinese stamp (No. 1164) shows the mother of Marshall Yueh Fei (1103-1141) tattooing four Chinese characters on his back, while

Figure 1

he patiently kneels. The characters "Ching Ching Pao Kno," mean "Supreme Loyalty to the State." She did this as a parting reminder to the young warrior before he fought and repulsed the invading Tartars, 800 years ago.

Imhotep, Vizier of Pharoh, was an historic figure who lived about 2900 B.C. He is credited with numerous accomplishments in diverse fields; among them, a successful physician who was one of the first medical men whose name was recorded. He subsequently became a god of medicine, identical in stature with the Greek physician-god Æsculapius. This Egyptian postage stamp (No. 153) shows a reproduction of a mural in the Imhotep temple at Philae. It shows him as a full deity, invested with the emblems of his position: the ankh (sign of life) in his left hand and the scepter of power in his right hand.

The next advance in medicine took place in Greece. Here it was also begun with magic and superstition. Æsculapius, son of the great physician Apollo, became so adept at healing that he interfered with the population of Hades. Æsculapius is usually depicted as an aged man with a beard, and, for centuries, he has been accepted by the medical profession as its titular head. Spain issued a postage stamp (RA-25) depicting Æsculapius.

Hippocrates (460-370 B.C.), known as the "Father of Medicine," was an Aesclepiad

of the temple at Cos, one of the Dodecanese Islands. His statue is shown on a Greek postage stamp (No. 514). Medicine is indebted to Hippocrates for many things—particularly, for his initiation of clinical examination and observation. These procedures are perhaps of greater importance in dermatology than in any other field of medicine because, in many cases, the identification and cause of a disease is dependent upon observation and deduction. The "Hippocratic Collection," a group of volumes printed in Alexandria about 100 years after the death of Hippocrates, contributed much to the history of dermatology, since it focused great attention on diseases of the skin.

The Greek philosopher and physician, Aristotle (384-322 B.C.), wrote on metaphysics, natural science, ethics, politics, rhetoric, and poetry. He also introduced the practice of dissection, the use of anatomical drawings, and the study of anatomy and embryology (Greece, No. RA 91).

The Arabian physicians also made many contributions to dermatology, particularly in their accounts of leprosy and elephantiasis. Diseases of the scalp were carefully described by Avicenna (A.D. 980-1037). He remained an "authority" on diseases of the skin throughout the Middle Ages and described anthrax (Persian fire), carbuncles, and rubella, or German measles, as well as icthyosis, favus, impetigo, pediculi and their ova, warts, pigmentation of the skin and nails, and scar formation (Iran, No. B32).

Maimonides (A.D. 1135-1205), a Jewish rabbi and physician, was born in Spain. He wrote extensively on hygiene, law, philosophy, and medicine and was the first to attempt to systematize and index the vast accumulation of material pertaining to Jewish laws. His best-known contribution to medicine consists of his work on sexual hygiene. He was honored by Israel on a postage stamp issued in 1953 to commemorate the Seventh International Congress for the History of Science (No. 74).

The revival of learning, fall of Constantinople, invention of printing, epic geographic discoveries beginning with Columbus, studies in astronomy and physics by Copernicus (Poland, No. NB 23) and Galileo (Italy No. 421), and the works of Leonardo, Vesalius, Fracastro, Santorio, and numerous other lesser geniuses, indicated that the interest in biologic science was not surpassed by other advances.

Much of this interest can be allocated to dermatology, since cutaneous diseases have constituted one of the major interests in medicine from the beginnings of recorded history.

Two outstanding contributors to medicine at this time were Andreas Vesalius (1514-1564) and Ambroise Pare (1510-1590). Vesalius is considered to have been one of the outstanding anatomists of all time and through his studies established a basis of present-day anatomy. His illustrous volume, "De Humanis Corporis Fabrica," was written before he was 30 years of age (Belgium, No. B320). Pare, the leading surgeon of his generation, described scabies as, "The mites are little animals, always hidden under the skin, there they crawl and gnaw the skin, little by little, exciting a disagreeable itching. They can be extracted with pins or needles."

Van Helmont relinquished his study of philosophy to devote himself to medicine and study the works of Galen. However, one day he accidentally "picked up" the glove of a woman who had scabies, and he contracted the condition. He then treated himself according to the instructions of Galen, who believed the condition was due to a "combustion of the bile," and "a saline state of the phlegm." Therapy apparently consisted of drastic purgation. Van Helmont followed these instructions dutifully and became extremely "weakened," but the condition of his skin did not improve. He became disillusioned with the so-called "healing-art," and "regretted that he sacrificed both time and station in descending to it, gave his library to students, and affected sorrow

Figure 2

afterwards that he had not burnt it, so angry was he with physic" (Meryon). He eventually "cured" his "itch" with remedies prescribed by Paracelsus, for whom he then became enthusiastic and determined to follow in his "footsteps" and to dedicate his life to the reform of medicine (Belgium, No. B322).

Leprosy (Fig. 2).—The recognition of leprosy resulted in two advances in medicine. First, the establishment of hospitals and advancement of nursing, and, second, a new emphasis on the objective study of disease (particularly diseases of the skin), such as that which occurred for syphilis 500 years later.

In Brazil, the first hospital for patients having leprosy was founded by a missionary, José Anchieta (1534-1579). A leprosarium of 500 beds had been organized by Gregor von Tours (A.D. 538-594), known as St. Gregory of Tours, who studied medicine when he was a "young" man and who wrote on subjects pertaining to medicine.

The lepra bacillus was discovered by Armauer Hansen (1841-1902) in 1872. His recommendation that patients with leprosy be isolated has tended to reduce the

incidence of the disease. His portrait appears on the Cuban postage stamp (No. 414) which was issued in 1948 to commemorate the International Leprosy Congress in Havana. Other physicians who have contributed to the knowledge of leprosy include Victor Babes (1854-1926), who in 1898 did bacterial investigations of the lepra bacilli and studies concerning the histology of the disease. He also wrote the section on leprosy for Nothnagel's "Handbuch" in 1901 (Romania, No. B355). Rudolph Virchow (1821-1902) contributed to research on leprosy and wrote five articles on the history of the disease (Germany, No. 9N89). In 1913 Albert Schweitzer (1875-) founded a leper colony and hospital at Gabon (Monaco, No. 236).

Belgium and Brazil have honored Father Damien, a Belgian missionary, who devoted his life to the cause of leprosy. He served many years at the leper colony on Molokai Island, Hawaii, and he died from the disease (Belgium, No. B417, B419, and Brazil, No. RA2).

On May 12, 1957, France honored the Knights of Malta for their work in French Equatorial Africa with patients having leprosy. The leper colony is pictured on a French postage stamp (No. 797). French Equatorial Africa issued a postage stamp (No. 194) showing the Leprosarium at Mayumba, and French West Africa issued one (No. 74) depicting a mobile leprosy clinic.

In 1938, a series of stamps were issued by Egypt to commemorate the International Congress of Leprosy. This shows the hydnocarpus plant, the source of chaulmoogra oil.

The one-pence stamp, issued by the Tonga Island in 1897, shows the breadfruit Artocarpus. The natives applied the roots of this tree externally for the treatment of leprosy.

Other countries have also used the "surtax" form of postage in their fight against leprosy. These include stamps from Dutch New Guinea (B7), which shows a leprosarium, and from Italian Somaliland (No. 195) and Suriname (No. B47).

Dermatology (Fig. 3).—During the years 1500 to 1750 the knowledge of dermatology progressed rapidly, as a result of studies by such investigators as Paracelsus, Fernal, Falloppio, Pare, and others.

That France became preeminent in dermatology was due, in part, to the fact that the Hôpital St. Louis (France, No. B285), in Paris, became a dermatologic institution, thereby furnishing a center for the study of cutaneous diseases.

Dermatology had been considered to be a part of general medicine from early antiquity to comparatively recent times, but during the past one and one-half centuries its study and literature have been the work of specialists. Therefore, the history of dermatology can be separated from that of internal medicine only since the end of the 18th century.

During the latter one-half of the 18th century an effort was made to organize and classify cutaneous diseases and to introduce a more rational nomenclature. This attempt was undoubtedly fostered by the work of Linneaus, who provided a basis for the classification of plants.

Botany was the prime interest of Carl von Linne (1707-1778), who classified plants according to the character of the stamens and pistils. This classification became known as the "sexual system" and exerted an influence on science. He also classified the mites (Sweden, No. 294).

Von Liebig (1803-1873), a chemist, made an important contribution to the physiology of human beings with his classification of the basic foods contained in carbohydrates, fats, and proteins (Germany, No. 695).

The French physiologist Claude Bernard (1813-1878) was considered to be one of the first endocrinologists. He demonstrated the function of the pancreas and the effects of pancreatic juice. The foundation of our present knowledge of diabetes is believed to have been the result of his work on glycogenic function. He was also the first to demonstrate the nervous control of the

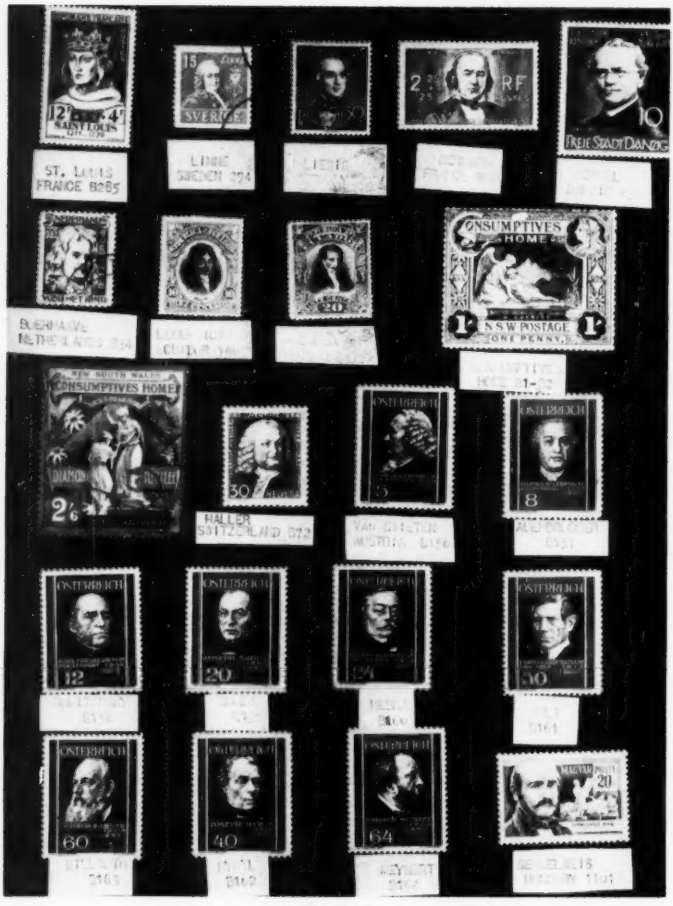


Figure 3

circulatory system, which included the presence of vasoconstrictors and vasodilators (France, No. 89).

Although he was not a physician, the work of Gregor Mendel (1822-1884) influenced the course of medicine. His investigations on "inbreeding" began with peas and beans, and he traced the fundamental laws of heredity to many psychic and physical diseases. This stamp is inscribed "Happy Children, Happy Future" (Danzig, No. 238).

Herman Boerhaave (1668-1738) was the first physician to be honored on a postage stamp for his accomplishments in medicine. This stamp was issued in 1928 (Netherlands, No. B34). Previously, in 1899, two physicians, Espejo (Ecuador, No. 141) and Leguerica (Ecuador, No. 140), had been similarly honored, but for their political accomplishments rather than for any contribution to medicine. In 1897, New South Wales, in commemoration of the Diamond Jubilee of Queen Victoria, issued a set of two stamps (No. B1, B2). These were the first "semipostal" issued by any country and were the forerunners of many thousands of similar ones. The difference between the revenue from these stamps and their postal value was donated to a "Home of Con-

sumptives." Boerhaave is also reputed to have laid the foundation for our modern medical clinics, since prior to the 17th century there was no clinical instruction and all universities conferred a medical degree on the basis of an oral dissertation. In 1701, he instituted clinical or "bedside" instruction, and he was also the first to use the fever thermometer. His pupils included von Swieten and von Haller (Switzerland, No. B72). Von Swieten (1700-1772), a Dutch physician and scholar, was called to Vienna by Maria Theresa. There he furthered the old Vienna School of Medicine, which was patterned after the medical faculty at Leyden (Austria, No. B156).

In 1937, Austria honored nine eminent physicians of the old Vienna school by issuing postage stamps having their portraits:

1. Conrad von Swieten, founder of the old Vienna School of Medicine (No. B156)
2. Leopold Auenbrugger, first to use percussion as a procedure in diagnosis (No. B157)
3. Karl von Rokitansky, performed more than 30,000 autopsy examinations and contributed a voluminous amount of material pertaining to pathology (No. B158)
4. Joseph Skoda, whose name is given to the rales present in pneumonia (No. B159)
5. Ferdinand von Hebra, founder of the school of dermatology (No. B160)
6. Carl Ferdinand von Arlt, whose treatises were a great aid in establishing ophthalmology as an independent speciality (No. B161)
7. Joseph Hrytl, the first eminent teacher of topographic and regional anatomy (No. B162)
8. Theodor Billroth, who initiated modern visceral surgery (No. B163)
9. Theodore Meynert, an eminent neurologist and psychiatrist, who did extensive investigations on the anatomy and physiology of the brain (No. B164)

One of the outstanding accomplishments of the Vienna School was the furtherence of medical specialties, such as dermatology and syphilology. During this period patients with cutaneous diseases were supervised by the department of chest diseases, of which Skoda was "chief." Those having dermatologic conditions were confined to an annex called the "Scabies Station," since all chronic diseases of the skin were then classified as scabies, regardless of the symptoms. No consideration was given to the nature or severity of their condition, and those having syphilis or mental diseases were also included. Von Hebra assumed charge of the cutaneous diseases, and, in 1845, this department was separated from that of diseases of the chest, thus initiating dermatology as a separate branch of medicine. Owing to his efforts, von Hebra is considered to be the founder of modern dermatology.

The relationship between contamination from the hands and puerperal infection was demonstrated by Ignaz Semmelweis (1818-1865) when he required that all attendants at the clinic wash their hands in a solution of calcium chloride. The institution of this procedure resulted in an impressive decline in the mortality rate. These findings were published by von Hebra, editor of the leading Vienna Medical Society Journal, in 1847, and Rokitansky and Skoda supported these findings. However, the majority of physicians, such as Klein, Semmelweis' "chief" at the clinic, were not impressed with his work (Hungary, No. 1101).

Allergy and Immunology (Fig. 4).—Although Harvey was best known for his discovery of the circulation of the blood, he was also a pioneer in experimental dermatology. In his "De Generation Animalium" he stated: "Having for tryal sake prickt my hand with a needle, I rubbed the point of the same needle with the tooth of the spider, and perforated the skin threw it in another part of my hand, but could distinguish no difference in the sense of the punctures, however, there was one remarkable enough in the skin; the invenom'd puncture, the same was soon raised up into a tubercle, looking red with heat and inflammation, rising up as it were to shake off the inflicted Evil." His experiment demonstrated the effect of inoculating a poison into the skin, resulting in an urticarial or erythematous reaction (Russia, 1947).

Emil von Behring (1854-1917) may be referred to as the "father of serum therapy." In 1901, he was awarded the

Figure 4

Nobel Prize for his work. This stamp, inscribed in German, stated: "To the Conqueror of Diphtheria" (Germany, No. B186).

Great insight into allergy was gained by the studies of P. J. Portier and R. C. Richet (1850-1935), in 1903. These first studies stemmed from the gaming tables of Monte Carlo. They accompanied Albert I, Prince of Monaco, on an ocean cruise and began their studies of extracts of a poison contained in the nematocysts of the physalia, a jellyfish which floats on the surface of the ocean and is related to the Portuguese man-of-war. These studies were subsequently continued in the laboratory and resulted in the discovery of anaphylaxis (Monaco, No. 303).

G. Widal (1862-1929) is best known for the Widal test, which is an "agglutination for typhoid fever using a living agglutinable culture of the typhoid bacillus as an antigen." His investigations also included studies on anaplylactic shock (France, No. 866).

In 1956, a postage stamp (No. 1080) was issued in the United States to honor H. W. Wiley. In 1906, while chief chemist of the Department of Agriculture, he was in-

strumental in bringing about the pure food and drug laws.

Bacteriology and Pathology.—The recognition of contagion was noted in the early history of medicine and the concept that contagion is due to a living virus, capable of reproduction (a contagion vivum), is an old one. This fact has stimulated dermatology more than other theory, since scabies and animal parasites, as causes of cutaneous disorders, furnished the first examples of diseases produced by demonstrable living organisms. The theory that contagious diseases are due to micro-organisms was clearly developed by Fracastoro, who had a marked interest in the study of syphilis and cutaneous diseases. He was the first to suggest that epidemic diseases were transmitted by contagion and caused by a micro-organism or "animalculae."

With the advent of bacteriology it was demonstrated that many diseases were caused by specific invasion of bacteria. The greatest aid to this fundamental science was the advent of the microscope. Anton Leeuwenhoeck (1632-1723) is credited with inventing the first useful microscope (Netherlands, No. B97).

Agostino Bassi (1773-1856) (Italy, No. 640), a pioneer in micropathology, introduced the concept of modern bacteriology in 1834. He wrote on the parasitic theory of disease a decade before the work of Pasteur. He was the first to demonstrate that the disease of silkworms was due to a micro-organism, a living vegetable parasite, and these studies led to finding the cause of favus (Achorion Schoenleini) in 1893. He was the first to note the associations of vegetable parasites with diseases of the skin in human beings.

In 1884, Koch demonstrated and cultured the tubercle bacilli in lupus vulgaris and was able to transmit the infection to animals and to cultivate the organism from lesions in these animals, thus fulfilling the postulates he had outlined (Belgium, No. B554).

A vast amount of the pioneer work in bacteriology was done by Louis Pasteur (1822-1895). He demonstrated that bacteria are living organisms, against which an immunity can be "produced." In 1877, after 20 years of research on the biology of micro-organisms, Pasteur extended his studies to include diseases which affect higher animals and human beings. His first investigations were on anthrax, chicken cholera, and rabies. In 1878-1879, he was able to demonstrate the streptococci and staphylococci (France, No. B53).

The demonstration of phagocytosis, by Metchnikow, of the Pasteur Institute, showed that the cells also played an important role, not only by producing antibodies but by ingesting and destroying the invading bacteria.

Dermatology has also played a significant role in the history of bacteriology. In 1871, Hansen demonstrated the bacillus of leprosy. This was 11 years before Koch succeeded in isolating tubercle bacilli which was, according to Jordan, "one of the earliest observations of pathogenic bacteria."

In 1880, Laveran had observed the plasmodia of malaria (Algeria, No. 252), and, in 1897, Ross found that these plasmodia were transmitted by mosquitos which were identified as anopheles by Grassi, in 1898 (Italy, No. 701). In 1909, Walter Reed (United States, No. 877) and his associates clearly demonstrated that yellow fever is transmitted by a mosquito (Aedes aegypti) (Panama, No. C120). In 1909, Nicolle showed that typhus is transmitted by the body louse, which also transmits trench fever and relapsing fever (Tunis, No. 229).

In 1889, Edward Nocard (1850-1903), a French veterinarian and biologist, who was an assistant to Pasteur, discovered the virus of psittacosis. He described a genus of fungi known as Nocardia. The disease was named for him (nocardiosis) but is now included with the actinomycetes (France, No. 655).

Two important findings in the field of serum therapy were described by Behring, in 1890. One was that the body is able to

produce antitoxins for tetanus and the other that effective diptheria antitoxins could be produced which, when injected, neutralized the toxins. Ehrlich also did important studies on antitoxins and immunity, and he called the procedure described by Behring "passive immunization."

Johanne Purkinje (1787-1869) was a microscopist and experimental physiologist whose principal contributions were in embryology, histology, and ophthalmology. He was the first to describe the ciliary movements in cells, and he introduced the term "protoplasm." He also stressed the value of fingerprints as a means of identification, and he is reputed to be the first to use the microtome, glacial acetic acid, and Canada balsam. He was the first to describe the sweat glands ("Purkinje's gland of sudoriferous variety"), and his name is given to seven or eight anatomic structures (Czechoslovakia, No. 230).

Victor Babes (1854-1926), in collaboration with Schwimmen, wrote the section on "New Formations of the Skin" in Ziemssen's "Handbuch." He was professor of bacteriology and pathologic anatomy at Bucharest. In 1889, he did bacteriologic investigations of septic processes in infants, and, in 1925, on giant cells, as well as studies on leprosy. In 1882, he wrote "Eine experimentelle Studie ueber Einfluss des Nervensystems auf die pathologische Veranderungen der Haut" (Romania, No. 999).

Herman Boerhaave (1668-1738) described the true structure of the sebaceous glands as "cryptae sebacae."

In 1846, Rokitansky, then the undisputed leader in pathologic anatomy, published the first volume of his "Handbook of General Pathological Anatomy" (Austria, No. 592).

Rudolf Virchow (1821-1902) is regarded to have been the founder of modern pathology. When he was 26 years of age, he began the well-known *Archives of Pathologic Anatomy,* which came to be known as *Virchow's Archives.* His numerous experimental studies and discoveries include those on embolism and thrombosis (he coined both terms), amyloid, hematoidin, myelin, connective tissue, inflammation, and tumors. He was the first to define leukocytosis and, in 1845, described leukemia as "white blood." He also defined fatty degeneration, cloudy swelling, and ochronosis. In 1850, he introduced the terms mycosis and dermatomycosis; in 1855, he described pathologic pigment, the anatomy of the hair follicle, and chronic pemphigus; in 1857, normal and abnormal pathology of the nails, and glanders, and, in 1860, onychomycosis, dermatomyositis, and syphilis. The studies of Virchow initiated the change from gross to microscopic anatomy in pathology. Pusey summarized these contributions as: "The interest in cutaneous pathology was stimulated by the large amount of study which was given to the subject by Virchow."

Radiation and Physical Therapy (Fig. 5).—The application of physics has had far-reaching results in dermatology, particularly in therapy. Although the invigorating effects of sunlight had been recognized since ancient times, Niels R. Finsen (1860-1904) was the first to devise a satisfactory apparatus for the production and application of ultraviolet light, thus, placing this form of therapy on a scientific basis. Between 1894 and 1897, he did the first fundamental physiologic studies of the effects of light rays on tissues, and his use of ultraviolet light for lupus vulgaris and other forms of tuberculosis opened a new field in therapy. He was awarded the Nobel Prize in medicine in 1903 (Danish Seal).

Although William Konrad Roentgen (1845-1923) was not a physician, it seems proper to include him in any dermatologic history because of his discovery of x-ray in November, 1895. The first Nobel Prize in physics was awarded to Roentgen in 1901. Postage stamps honoring him have been issued by Germany, Danzig, and Suriname. The Danzig stamp (No. 240) bears the inscription "Fight Cancer—Cancer is Curable."

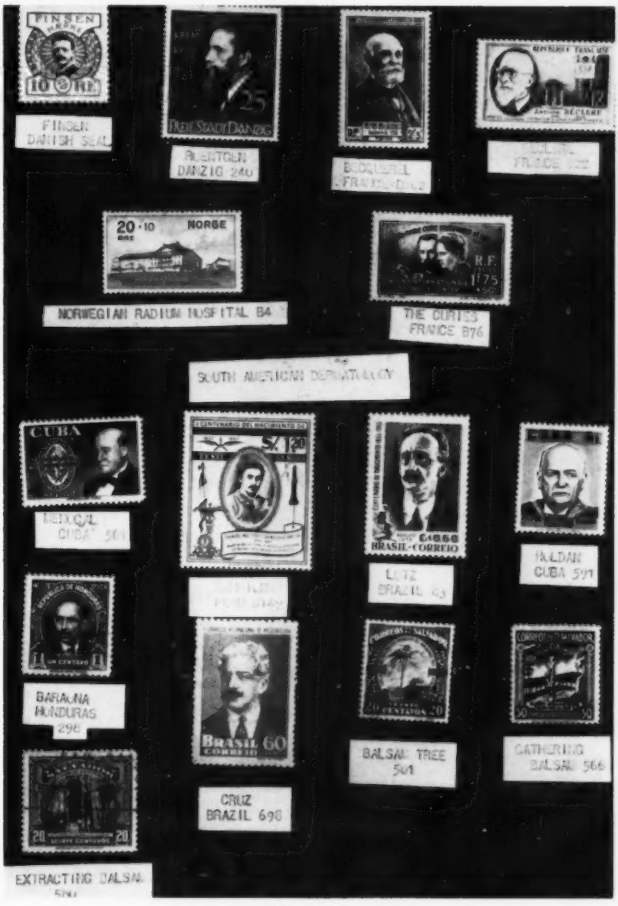


Figure 5

One year after the discovery of x-rays, Antoine Becquerel demonstrated natural radioactivity. His experiments with pitchblende led to the subsequent discovery and isolation of radium by the Curies. Becquerel's rays is sometimes used as a synonym for radioactive rays. The radium used at the Hôpital St. Louis for therapeutic studies on cutaneous diseases was the property of Becquerel (France, No. B202).

Anton Beclere (1856-1939), a pioneer radiologist, was regarded to be the founder of French radiology. He introduced roentgenotherapy for glandular tuberculosis (France, No. 822).

The experiments done by Madame Curie (France, No. B76), prior to her discovery of radium in 1898, are well known. Three years later, Becquerel carried a tube of radium in his pocket for a period of two weeks and subsequently noted an area of severe dermatitis on his abdomen. Therefore, Besnier suggested the possible therapeutic use of radium, and it was found to have the same effect as roentgen rays. These early experiments with radium were being done in Paris at the same time that Freund was developing roentgen-ray therapy in Vienna. The Norwegian Radium Hospital is pictured on a postage stamp (No. B4).

South American Dermatology (Fig. 5).—Ramimudo Menocal (1856-1917) studied in Madrid and subsequently received his medical degree at the University of Havana. He served as a very able Secretary of Public Health, during which time he was appointed to the Leper's Hospital at San Lazaro of Rincon. He became the founder of the Cuban School of Dermatology and trained some of our contemporary teachers. His "Treatise of Dermatology" has been used as a textbook (Cuba, No. 561).

Daniel Carrion, the son of a physician, was born in 1858. Although he did not become a physician, he became interested in the etiology of verruga peruana while a medical student. On Aug. 17, 1885, he was voluntarily inoculated with blood from a patient having verruga. He soon had the symptoms of Oroya fever and kept a careful diary in which he detailed all the symptoms until the time of his death, on Oct. 5, 1885. By his sacrifice, Oroya fever was proved to be a malignant form of verruga peruana. This disease is now known as "Carrion's disease" (Peru, No. C149).

Adolfo Lutz (1855-1940) was regarded as one of the greatest scientists of Brazil. In 1893, he was appointed director of the Sao Paulo Bacteriological Institute, which he transformed into a research center for the study and elimination of the epidemic diseases which were then hindering the progress and development of the state. South American blastomycosis, caused by Blastomyces brasiliensis, is still known as "Lutz's disease."

In 1907, F. D. Roldon (1864-1942), known as Cuba's "Father of Radiology," introduced radiology and radiotherapy to that country (Cuba. No. 591).

Baraona (1863-1937) gained an international reputation as the "chief" of the clinic for tropical diseases which he established at San Pedro Sula. He was President of Honduras from 1925 to 1929 (Honduras, No. 298).

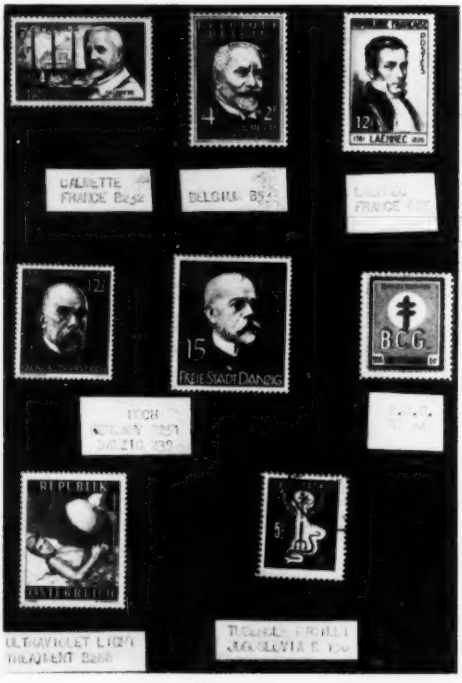


Figure 6

Oswaldo Cruz (1872-1917) was a physician and bacteriologist of Brazil. He was best known for his successful campaign against yellow fever in Rio de Janerio and for the establishment of the efficient public hygiene service of the Brazilian government (Brazil, No. 698).

Salvador is the smallest, most densely populated, and most extensively cultivated country in Central America. Several stamps issued by this country depict the balsam of Peru which is an important item of export. This misnomer occurred when Pedro de Avarado, one of Cortez' lieutenants who took part in the invasion of 1524, believed the country to be Peru. These stamps show the balsam tree (No. 501), gathering balsam (No. 566), and extracting balsam (No. 580).

Tuberculosis (Fig. 6).—Albert Calmette (1863-1933) was particularly interested in the study of tuberculosis and, together with Guerin, developed a method for the preventive vaccination of newborn infants (BCG) (France, No. B232; Belgium, No. B533).

In 1816, R. Laennec (1781-1826) became "chief" of the Necker Hospital where he devised a rational system for diagnosis of diseases of the heart and lungs. His invention, the stethoscope, facilitated diagnosis by means of ausculation. His "Traite de L'Ausculation Mediate," published in 1819, has probably done more to advance the art of diagnosis than any other single publication (France, No. 685).

The striking originality of Robert Koch's (1843-1910) work is well illustrated by his postulates, research on cholera, and dis-

Figure 7

covery of the tubercle bacillus, culture media, and tuberculin. He was honored on postage stamps by three countries: Germany, Danzig, and Belgium. The Danzig stamp is inscribed "Fresh Air and Sunshine, the Enemy of Tuberculosis" (Germany, No. B251; Danzig, No. 239).

Many countries have issued postage stamps to publicize the campaign against tuberculosis. A stamp from the Dominican Republic (No. RA 24) is inscribed "B. C. G." (Bacillus Calmette-Guerin). One issued in Austria (No. B288) shows a patient under a sun lamp. Note the tubercle bacilli shown on the stamp, depicting a dying serpent which was issued in Jugoslavia (No. B 150).

Syphilis (Fig. 7).—Leprosy was rapidly subsiding during the latter part of the 15th century and was soon to disappear in Central Europe. However, in the latter half of this century, it was followed by a new plague, syphilis. This disease, which appeared suddenly, was more instrumental than any other factor in stimulating an objective study of disease and a search for its etiology. Syphilis, which is a cutaneous disease in the same sense as leprosy, has occupied many of the most able minds of medicine from Paracelsus and Fracastro to Virchow and our present-day leaders.

The poem "Syphilis Sive Morbus Gallicus" was the crowning achievement of Fracastro (1483-1553). He described the disease and gave an accurate account of its incidence and course in the various countries of Europe, and he mentioned a heavy metal (mercury) as a therapeutic measure. This poem also contained other ideas regarding this disease (subsequently demonstrated by the works of Pasteur, Schaudin, and Fleming) and was a most remarkable contribution to the practical information and symbolic explanation of syphilis. He also mentioned the case of a young man who was apparently "cured" of the disease when a goddess bathed him in a "lake of silver" (Italy, No. 695).

Ambroise Pare (1510-1590) was considered to be the foremost surgeon of his generation. In 1568 he wrote "Traiete de la Peste, de la Petite Verolle et Rougeolle: Avec Une Briefue Description de la Lepre," which was the first description of syphilis in young children. He is credited with being the first to suggest transmission of the disease from an infected mother to her child. He also noted induration of the chancre and called attention to the characteristic indolence of the syphilitic bubo. He regarded mercury, administered by inunction, to be a specific form of therapy but was opposed to the use of mercury to the point of salivation. He also noted the relationship between aneurysm and syphilis.

In 1529, Paracelsus (1492-1541) wrote several articles on syphilis in which he advocated therapy with mercury, but he created confusion by designating the disease "French gonorrhea" (Germany, No. B311).

Boerhaave was also among those who contributed to the study of syphilis with the publication of his book, "Aphrodiacus," in 1782 (Netherlands, No. B107). G. von Swieten believed mercury to be specific for syphilis, and he employed inunction to the point of salivation. His "Spiritus Anti-Veneris of Mercuric Chloride" consisted of "one-half a drachm of mercuric chloride in one pint of wine" (Netherlands, No. B115).

In 1903, Roux (1853-1933) (France, No. B289), and Metchnikoff (1845-1916) (Russia, No. 1011) succeeded in the experimental transmission of syphilis from man to higher apes. Roux's principal discoveries were antidiphtheria and antitoxin serums for diphtheria, while Metchnikoff also described a prophylactic ointment for syphilis.

One of the best known syphilologists of the 19th century, Jean-Alfred Fournier (1832-1914), made contributions covering the entire field of syphilis. However, he is best remembered for his statistical establishment of the connection between syphilis and tabes, and for his introduction of bismuth as a therapeutic measure for this disease (France, No. B201). He was a clinical professor at the University of Paris from 1880 to 1905 and at the Hôpital St. Louis

from 1884 to 1905. His volume, "Traitement de la Syphilis," published in 1893, was translated into English in 1906.

In 1938, the Societe Francoide de Prophylaxie Sanitarie et Morale issued a postage stamp depicting the symbolic figure of France holding an infant in her arms (the future race), which was intended to aid in the campaign against syphilis (France, No. B64).

H. Noguchi (1876-1928) was a Japanese bacteriologist and physician who specialized in research on syphilis. He is best known for producing pure culture of the syphilitic organism and for his diagnostic tests for syphilis (Noguchi's leutin reaction for syphilis) (Japan, No. 480).

In 1854, R. Virchow (1821-1902) described the infiltrative changes, supposedly characteristic of syphilis, which occur in the organs and tissues. In 1860, he described the pathology of congenital syphilis, and his accounts of the course of syphilis and its distribution throughout the blood stream were the first clear interpretation of the various stages of activity and inactivity of this disease.

The many neurologists who contributed to the knowledge of syphilis include V. M. Bechterev, a Russian neuropathologist, best known for "Bechterev's sign" (anesthesia in the popliteal space in neurosyphilis and paresis) (Russia, No. 1655).

An important contribution to medical education was made by Julius Wagner-Jauregg (1857-1940) when he established pediatrics, psychiatry, and dermatology as separate required studies. His contribution to syphilology consisted of the therapeutic induction of malaria to patients having syphilitic involvement of the central nervous system (dementia paralytica). In 1927, he was awarded the Nobel Prize for "the discovery of therapeutic value of malaria inoculation in the treatment of dementia paralytica" (Austria, No. 615).

This stamp (France, No. B68) was issued to honor two physicians: a father and a son. However, the portrait is that of the son. The father, Jean Martin Charcot (1825-1893), was an eminent physician and "Charcot joints," which occur in syphilis, are recognized by every physician.

Woiciech Oczko (1537-1599) was honored on a stamp issued by Poland (No. 770) in 1957. He wrote many books on medical subjects, among them the first Polish monograph on syphilis, which was printed in 1581.

David Livingstone (1813-1873), a missionary and physician, described a disease which occurred in the Baratje and which was known as "manassah." He differentiated this disease from syphilis, although it was probably yaws. In 1955 Rhodesia issued a postage stamp in his honor (No. 157).

The name of Paul Ehrlich (1854-1915) instantly brings to mind his most important and practical contribution to dermatosyphilology: "606," also known as arsphenamine (Salvarsan). At that time, this drug was the most potent therapeutic measure known for the treatment of any infectious disease.

Ehrlich and Behring became close friends because of their work with diphtheria serum. They received a contract from a chemical factory giving them the financial returns from this discovery. However, Behring is reputed to have "tricked" Ehrlich out of his portion of the profits, and Behring's subsequent attempts to reconciliation with him were rejected. It required a postage stamp to reunite Ehrlich and Behring (Germany, No. 722).

In August, 1957, Sweden issued a postage cancellation honoring the Tenth International Congress of Dermatology (Fig. 8).

Figure 8

Because postage stamps are one means for a country to pay honor to its physicians, the history of dermatology is being recorded in this manner. It is possible, in the not too distant future, that a complete history of dermatology may be recorded on postage stamps.

30 N. Michigan Ave.

BIBLIOGRAPHY

Ackerknecht, E. H.: A Short History of Medicine, New York, The Ronald Press Company, 1955.

Adams, F.: The Genuine Works of Hippocrates, Baltimore, The Williams & Wilkins Company, 1939.

Bennett, R.: The Diseases of the Bible, London, Religious Tract Society, 1887.

Dowdy, A. N., and Warren, S. L.: Seventy-Five Years of Medical Progress, edited by L. H. Bauer, Philadelphia, Lea & Febiger, 1954.

Finnerud, C. W.: Ferdinand von Hebra and the Vienna School of Dermatology, A. M. A. Arch. Dermat. & Syph. 66:223 (Aug.) 1952.

Fox, H.: Dermatology of the Ancients, J. A. M. A. 65:469 (Aug. 7) 1915.

Gelfand, M.: Livingstone the Doctor, Oxford, Blackwell Scientific Publications, 1957.

Gottfried, O.: Doctors Philatelic, New York, American Physician, Inc., 1954.

Kaposi, M.: Pathology and Treatment of Diseases of the Skin, New York, William Wood & Company, 1895.

Lake, N. C.: Tattooing in the Service of Surgery, Brit. M. J. 1:1084 (May 10) 1958.

McCaw, I. H.: A Synopsis of the History of Dermatology, Ulster M. J. 13:109 (Nov.) 1944.

Marquardt, M.: Paul Ehrlich, New York, Henry Schuman, Inc., Publishers, 1951.

Pinkus, H.: Paul Ehrlich and His Impact on Dermatosyphilology, A. M. A. Arch. Dermat. 72:113 (Aug.) 1955.

Pusey, W. A.: History of Dermatology, Springfield, Ill., Charles C Thomas, Publisher, 1933.
Disease, Gadfly to the Mind, Brit. J. Dermat. 46:341 (Aug.-Sept.) 1934.

Rayer, P.: Treatise on the Diseases of the Skin, London, G. Henderson, 1841.

Roddis, L. H.: Life and Influence of Hippocrates, Current M. Digest 23:26 (Dec.) 1956.

Sulzberger, M. B., and Witten, V. H.: Dermatology and Syphilology in 75 Years of Medical Progress—1878-1953, edited by L. H. Bauer, Philadelphia, Lea & Febiger, 1954, pp. 31-49.

von Klein, C. H.: The Medical Features of the Papyrus Ebers, J. A. M. A. 45:1928 (Dec. 23) 1905.

The Treatment of Scleroderma with the New Chelating Agent, Edathamil

SIGFRID A. MULLER, M.D.; LOUIS A. BRUNSTING, M.D., and R. K. WINKELMANN, M.D., Rochester, Minn.

The systemic forms of scleroderma are disabling entities included in the group of "collagen diseases" but, unlike others in the group, are unresponsive to steroids. The absence of a useful therapeutic agent in the treatment of scleroderma is a serious clinical handicap, especially since the incidence of scleroderma is probably greater than that of systemic lupus erythematosus, dermatomyositis, or periarteritis nodosa.

In a recent report, a new chelating agent, edathamil disodium (Disodium Versenate), was shown to have markedly beneficial effects in a case of advanced scleroderma with extensive calcinosis.[1] The intravenous administration of this drug in protracted courses led to definite clinical improvement, with dissolution of large quantities of pathologic calcification. In the past year, other reports attesting to the ameliorative effect of edathamil in scleroderma have appeared.[2-4] In this project our purpose has been to explore the effects of this new agent and to report our observations in 23 cases of scleroderma.

Review of Literature

Pharmacology.—Edathamil disodium, the disodium salt of ethylenediaminetetraacetic acid, is a potent chelating agent. It is referred to also as Endrate,* Versene, Versenate, Sequestrene, Nullapon, Calsol, and EDTA. Throughout the rest of this paper, the disodium salt will be referred to simply as edathamil.

This drug binds metallic ions in an inner ring, thereby deionizing and deactivating the metal. The resulting complex is water-soluble and virtually nondissociated. In vitro, metals form chelation rings in a descending order of stability as follows: lead, copper, nickel, cobalt, zinc, calcium, ferrous ion, manganese, and magnesium. Thus, lead will displace copper in a chelation ring, copper will displace nickel, and so on.

Foreman and Trujillo[5] have demonstrated that edathamil labeled with C^{14} carboxyl is transferred intact into the urine by both glomerular filtration and tubular excretion and that less than 1% is metabolized; 50% of an intravenously administered dose could be recovered in the urine in 1 hour and about 98% in 24 hours. It was found that the drug does not penetrate the erythrocytes and that it mixes quickly with all the body water, though diffusion into the cerebrospinal fluid was relatively slow. Only 5% of the drug was absorbed from oral administration and none from the skin. The latter observation is in disagreement with the findings of Popovici et al.[6] who observed significant absorption through the skin.

When edathamil is given intravenously, the calcium salt is the predominant formation. One gram of edathamil binds approximately 108 mg. of calcium in vitro. In vivo,

Submitted for publication Dec. 17, 1958.

Abridgment of thesis submitted by Dr. Muller to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Dermatology.

Mayo Clinic and Mayo Foundation. Fellow in Dermatology, Mayo Foundation (Dr. Muller); Section of Dermatology (Drs. Brunsting and Winkelmann). The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota.

* Furnished by Dr. George Berryman, Abbott Laboratories, North Chicago, Ill.

it is only 45% to 72% as efficient.[7] The remaining 28% to 55% may be partially bound to various other metals found in body fluids, probably in the order of descending stabilities. This explanation has been partially substantiated by Perry and Schroeder.[8]

Therapeutic Uses.—The sodium and calcium salts of ethylenediaminetetraacetic acid have been used medically against various diseases. A few of the many are angina pectoris and calcific valvular stenosis, hemochromatosis, lead poisoning, metastatic calcifications in the kidney, acute porphyria, retention of radioactive metals in the bodies of workers, and cardiac arrhythmias induced by digitalis. The substance is an effective anticoagulant in vitro, especially recommended for platelet transfusions. It is used routinely in many laboratories to decalcify bone for histologic study. Incorporated in an ointment, it has accelerated the healing of chrome ulcers and it has facilitated the removal of barium-enema impactions.

Toxicity, Side-Effects, and Complications.—Short-term experiments with animals indicate that edathamil has a low degree of toxicity, provided the rate of administration is slow enough to avoid tetany. If it is given rapidly intravenously, the concentration of serum calcium falls abruptly and death occurs quickly because of hypocalcemic tetany or cardiac arrest. At presently recommended dosage schedules in man, no tetany has been observed. Long-term administration of edathamil in rats and other animals has resulted in loss of weight and impairment of growth. In Drosophila, the addition of edathamil to the food supply resulted in growth failure and dwarfism. Foreman and associates have shown a predictable occurrence of nephrotoxic effects in rats directly related to the amount of edathamil administered, but they were not able to explain the susceptibility of the rats showing these changes.[9]

Dudley and co-workers[10] reported the postmortem findings from two human cases in which very large and protracted courses of edathamil had been given. Three main alterations were reported: (1) severe damage to the proximal convoluted tubules of the kidney, (2) engorgement of the reticuloendothelial cells with coarse eosinophilic granules, and (3) severe hemorrhagic manifestations. A sudden death from cerebral embolism during administration of edathamil has been reported.[11] Foreman and associates[9] reported one case in which signs of marked renal irritation developed during treatment with edathamil but subsided five days after administration of the drug was stopped.

Although the anticoagulant effects of edathamil were evident in one postmortem study,[10] other hemorrhagic manifestations have not been reported in the literature. Thrombocytopenia was reported in one case.[12]

In seven reported cases, dermatitis suggestive of vitamin B deficiency developed but subsided promptly on withdrawal of the drug and administration of vitamin B, which was particularly effective in the forms of pyridoxine and nicotinamide.[8,13]

Hypotension occurring during the intravenous administration of edathamil and lasting a few hours has been reported by one investigator.[14] However, large amounts of edathamil administered in unusually short periods were responsible.

Clarke and associates[11] have given more than 4,000 infusions of edathamil without complications, except for mild gastrointestinal upsets and local burning at the site of the infusion. Rarely did these necessitate stopping the infusion.

Manner of Administration.—The intramuscular administration of edathamil is too painful for use. Absorption from oral administration is slight, although recently Peters and co-workers[15] have reported that oral administration benefited some of their patients with porphyria. At the present time the intravenous method is considered the only one feasible. A large vein is best for it.

Foreman and associates[9] have recommended 50 mg. of edathamil per kilogram of body weight daily for five days, followed

by a two-day rest period before repetition of the dose. A daily maximum for any patient should be 5 gm.; our usual daily dose is 3 gm. The drug is dissolved in 500 ml. of 5% dextrose in water or isotonic saline and given intravenously in about four hours. Clarke[11] has given slightly larger doses in about two to four hours and, unlike others, usually has not hospitalized his patients. He has expressed the opinion that the in vivo action of edathamil persists long after its administration, even for as long as a year.

Materials and Methods

Scleroderma was classified as of three main types: *Diffuse Scleroderma*—central cutaneous sclerosis progressing peripherally, without vasospastic symptoms, but with evidence of involvement of other organs. *Acrosclerosis*—cutaneous sclerosis pronounced in the acral areas and spreading centrally, with vasospastic symptoms in the extremities. Further, cases of acrosclerosis were divided into severe and moderate groups according to (1) the degree of Raynaud's changes (ulceration, gangrene, and so on), (2) the extent of the sclerosis, and (3) evidence of visceral involvement. Those of questionable severity were grouped as severe. *Morphea*—forms of scleroderma limited to the skin, subdivided into (1) localized morphea, (2) widespread morphea, and (3) linear scleroderma.

Twenty-three patients with scleroderma of varying degrees were selected for treatment with edathamil. Twenty cases showed the predominant features of acrosclerosis; two were classified as diffuse scleroderma and one as widespread morphea. The youngest patient receiving edathamil was 12 years of age, and the oldest, 67.

All the patients were hospitalized. Dosage schedules were modified in accord with the general recommendations of Foreman and associates[9] and Clarke.[11] Three patients were given a second course of edathamil after an interval of six to eight weeks.

Vital signs were checked during and after the infusions of edathamil. Some of the patients received 50 mg. of pyridoxine and 200 mg. of nicotinamide daily and for considerable periods thereafter. In addition to the routine admission laboratory tests, urinalysis was performed daily in all cases. Detailed studies of blood and of urinary calcium and phosphorus were made in eight instances, and in several cases bleeding, clotting, and prothrombin times also were checked at periodic intervals.

During the course of treatment, the patients' subjective evaluations were noted periodically. None of the patients became worse during treatment. Almost all thought themselves improved. By objective criteria, 7 of 15 patients with severe acrosclerosis and 1 of 5 patients with moderate involvement improved significantly and 1 of 2 patients with diffuse scleroderma experienced significant amelioration but the 1 patient with widespread morphea received no benefit. Objective evaluation of improvement depended mainly on performance in certain functional tests, such as crossing the legs, making a fist, and opening the mouth. Apparent changes in the degree of sclerosis were recorded. In order to gauge improvement more accurately, studies in esophageal motility[16] were carried out in several of the cases before and after chelation. Three patients had skin biopsies before and after treatment with edathamil, but the changes were not clearly evident and were difficult to interpret.

Report of Cases

The longest of the follow-ups has been two years, most having extended only a few weeks to a few months. Our experience in the treatment of scleroderma with edathamil is summarized in the Table. Following is a résumé of each of the nine cases in which significant improvement was noted objectively.

Case 1.—The cutaneous sclerosis was moderately softened, and the range of motion of the extremities was markedly increased. A second course of treatment eight weeks after the first brought no further improvement. One year later the patient relapsed and was again much worse. A follow-up letter two years after the first treatment with edathamil stated that she had improved greatly again as a result of using an amino acid supplement.

Case 7.—The patient experienced a remarkable improvement. Her skin returned practically to normal; pinching of the facies was lessened; dysphagia was decreased, and the severity and frequency of the occurrence of Raynaud's phenomenon in her hands were greatly reduced. Her dentist noticed that it was much easier to work on her teeth because of her increased ability to open her mouth. The severe contractures of the fingers were not affected, and ulcers have continued to develop on the fingertips. The improvement continued for several weeks after chelation. There has been no exacerbation of symptoms in 10 months of follow-up.

Case 8.—The treatment was given during the edematous phase of the disease. After about one week of administration of edathamil the edema disappeared, the sclerosis decreased, and the range of motion of the extremities was extended. Comparison of tracings of esophageal motility made before

Results of Treatment with Edathamil in Twenty-three Cases of Scleroderma

No.	Age	Sex	Diagnosis	Duration	Severity (0-4)	Total Edathamil, Gm.	Improvement, %	Complications
1	18	F	Acrosclerosis	5 yr.	++++	112	50	Burning in arm; transient diplopia & dyspnea
2	59	M	Diffuse scleroderma	1 yr.	++++	111	0	Slight renal irritation
3	67	F	Widespread morphea	7 mo.	++	38	0	--
4	43	M	Acrosclerosis	8 yr.	++++	42	0	Burning in arm
5	58	F	Acrosclerosis	5 yr.	++	49	0	--
6	52	F	Acrosclerosis	1 yr.	++	49	0	Burning in arm
7	31	F	Acrosclerosis	10 yr.	++++	54	75	Burning in arm; slight renal irritation
8	43	F	Acrosclerosis	9 mo.	++++	107	50	Burning in arm; anorexia
9	30	M	Acrosclerosis	2 yr.	++++	50	75	Mild chemical phlebitis
10	57	F	Acrosclerosis	2 yr.	++++	48	50	Slight renal irritation; mild chemical phlebitis; anorexia
11	47	M	Diffuse scleroderma	16 mo.	++++	50	25	--
12	43	F	Acrosclerosis	1 yr.	++	50	0	Slight renal irritation
13	41	M	Acrosclerosis	3 yr.	++++	49	0	--
14	49	F	Acrosclerosis	1 yr.	++	50	25	Burning in arm
15	26	F	Acrosclerosis	2 yr.	++++	45	0	Slight renal irritation
16	34	F	Acrosclerosis	1½ yr.	++++	50	0	--
17	53	F	Acrosclerosis	8 yr.	++++	47	25	--
18	54	F	Acrosclerosis	7 yr.	++++	49	0	--
19	27	F	Acrosclerosis	6 mo.	++	39	0	Mild renal irritation
20	12	F	Acrosclerosis	2 yr.	++++	40	50	--
21	48	M	Acrosclerosis	2 yr.	++++	50	0	--
22	36	F	Acrosclerosis	2 yr.	++++	37	0	Marked renal irritation & pustular dermatitis of mouth
23	40	F	Acrosclerosis	18 yr.	++++	50	0	--

this therapy with others made six weeks after showed improvement in the coordination of the contractions and in the relaxation of the gastroesophageal sphincter during deglutition. A second course of edathamil six weeks later resulted in no further improvement. In seven months of follow-up the patient has remained about the same.

CASE 9.—The patient showed marked improvement, particularly noticeable on follow-up five months after treatment. His face had lost much of the pinched appearance, and his skin was much softer. In the two months prior to chelation, he had had much dysphagia with episodes of emesis. The dysphagia improved greatly with treatment, and the patient has not vomited since receiving the edathamil. Comparison of esophageal motility tracings made before the use of edathamil, immediately after, and five months later revealed no change. At the latter time, the patient was able to open his mouth much wider than before and he had gained several pounds. He had resumed his occupation as a truck driver.

CASE 10.—The cutaneous sclerosis softened moderately, and the range of motion increased greatly. Although this patient had no dysphagia, a study of esophageal motility revealed marked involvement of the esophagus. Comparison of the esophageal motility tracings made before and after treatment demonstrated marked improvement. The patient continued to improve subjectively in the month following chelation. A follow-up letter four months after treatment stated there had been no further change.

CASE 11.—The patient had had diffuse scleroderma for 16 months. He experienced only a little softening of the cutaneous sclerosis after treatment. Comparison of the esophageal motility tracings made before and after chelation showed remarkable improvement, and there was great clinical improvement in the associated dysphagia. This patient had a duodenal ulcer which was unaffected by treatment. Improvement in his case is all the more significant because he had been given steroids for several months without betterment, and this measure had been discontinued during treatment with edathamil. A follow-up letter one month after the end of chelation stated that the patient had gained a few pounds but had not improved further.

CASE 14.—The improvement in this case was more clearly evident three months after chelation. Immediately after treatment with edathamil it was noted that the patient could make a better fist and could wring out a washcloth (which latter she had been unable to do). Three months later, her sclerosis was noted to be definitely decreased and the arthralgia that formerly affected her hands had disappeared.

CASE 17.—Acrosclerosis in this instance had an unusual pattern, with marked involvement of the entire gastrointestinal tract but only minimal in-

volvement of the skin. The patient had experienced severe episodes of vomiting, bloating, and obstipation. Gastroenterostomy had been attempted elsewhere without improvement. During the treatment with edathamil, the heartburn and constipation greatly improved. Comparison of the esophageal motility tracings made before and after this treatment revealed no change.

CASE 20.—The onset of acrosclerosis had occurred at the age of 10 years in one of the youngest patients we have observed with this disease. The progression of the cutaneous sclerosis was such that at age 12 years it was almost universal. Findings in esophageal motility studies were markedly abnormal, although appearances in the esophageal roentgenograms were normal and the patient had no dysphagia. Her condition improved considerably during treatment with edathamil: The skin of the dorsa of the hands and forearms softened, and the range of motion of the extremities increased greatly. The contractures of the hands were unaffected. At the end of treatment a repetition of the esophageal motility study showed little change from the previous tracing.

Usually the improvement in these patients was observed during the second week of treatment and gradually became more noticeable, reaching its peak at the conclusion of treatment or shortly thereafter. In two patients marked improvement continued for several months. The three patients who had a second course of treatment with edathamil six to eight weeks after the first showed no further change.

Recent reports have indicated that supplemental vitamin therapy during treatment with edathamil may be beneficial therapeutically. In our series, eight patients were given 50 mg. of pyridoxine and a therapeutic vitamin capsule daily. Of these, three improved. A second group of 11 patients were given 50 mg. of pyridoxine and 200 mg. of nicotinamide daily; and of these, three improved. A third group of four patients were given no supplemental vitamins, and three improved.

Calcinosis of the hands in two cases was not affected by treatment.

Two of the patients who had severe degrees of involvement died subsequently, one four months and the other seven months after treatment. The first had had electrocardiographic changes before treatment, and death was caused by sclerodermatous heart involvement. In the other patient, death was probably the result of scleroderma of the heart and kidney.

The commonest complication of edathamil treatment was burning at the infusion site. This was usually of mild degree and was more noticeable at the beginning of the course of treatment. Ordinarily, the burning pain was relieved promptly by slowing of the rate of infusion.

The only significant complication was renal irritation. In six patients, mild albuminuria occurred the last few days of treatment but was of no consequence. In one other case (a 36-year-old woman with acrosclerosis, Case 22), it was necessary to discontinue the use of edathamil after a total of 37 gm. had been given in a 13-day period. Severe albuminuria with granular casts and a transient mild increase in blood urea had occurred, and concomitantly the temperature rose to 101 F and an unusual pustular reaction appeared on the buccal mucosa. Cultures of the urine, blood, and material from the throat were negative. One week later the patient was asymptomatic and the urine showed only occasional casts. The pustular reaction on the buccal mucosa cleared in three days without specific therapy. In the two weeks preceding this reaction the patient had been given daily pyridoxine 50 mg., nicotinamide 200 mg., and a therapeutic vitamin capsule.

We observed no conclusive relationship between the dosage of edathamil per kilogram of body weight and the development of albuminuria. Several of our patients without abnormal urinary findings tolerated in the same time interval much larger doses than those in whom albuminuria developed. The finding of renal irritation is in contrast to the observations of others who have given similar dosages. It may have occurred because we gave only two or three rest days during the course of treatment instead of four, as recommended by others, or because our total dosage was slightly greater. If these differences are important, then the margin of safety for this drug is very narrow in susceptible persons.

Two patients had mild preexisting renal disease evidenced by mild albuminuria and casts prior to treatment with edathamil but tolerated the drug well. Two patients had mild chemical phlebitis at the infusion site lasting one or two days but without consequence. In the last week of treatment anorexia developed in two but cleared after a few days. One patient had a minor episode of vomiting, and one had transient diplopia and dyspnea after an infusion. Except for the renal irritation, all the complications were considered unimportant.

Results of the calcium balance studies done in eight of these cases are reported elsewhere.[17] They showed that edathamil is 69% to 92% effective in the binding and excretion of calcium. No abnormality in serum or urinary calcium was observed prior to chelation. Only mild transient hypocalcemia was noted during the administration of edathamil, with no evidence of clinical or latent tetany. The serum magnesium was unaffected by chelation in two patients.

Comment

From the beginning of our investigation it was recognized that evaluation of improvement would be extremely difficult. One has only to peruse the enormous amount of literature on successful treatment of scleroderma to be made doubly cautious and skeptical. In a study requiring intravenous medication and hospitalization, the use of controls is extremely difficult. In our investigation it was not done, and accurate statistical comparison, therefore, was not possible.

The difficulty of evaluating this new drug in scleroderma is the more evident since it has become apparent that the effects are not curative but ameliorative. Furthermore, scleroderma is known to have periodic flares and remissions, and therefore evaluation of changes induced by edathamil depended on the development of an unusual degree of improvement within a short time.

To us, edathamil seemed most useful in cases of acrosclerosis of severe degree. However, in no case was the drug curative, and whether edathamil influences the course of the disease remains to be proved. The two deaths in our series seem to indicate that this may not be the case. The known and unknown effects of this potent chelating agent appear to disqualify it from use against the benign cutaneous forms of scleroderma. Why improvement should have occurred in only nine of our patients is unexplained.

Complications in the administration of this drug were minimal. Because of the occurrence in seven cases of renal irritation—the only potentially serious untoward effect encountered—it is recommended that urinalysis be done every day while a patient receives edathamil intravenously and that administration of the drug be discontinued while albuminuria is present. As mentioned, mild, preexisting renal disease in two patients had no important effect.

Although no signs of vitamin deficiency developed in our patients, it probably is best to give supplemental vitamins during treatment. We could detect no potentiating therapeutic effect from the administration of pyridoxine and nicotinamide.

From our calcium-balance studies reported elsewhere,[17] it was estimated that the total amount of calcium removed from the body was at the most 10 to 20 gm. This is a small amount compared to the reservoir of at least 100 gm. of calcium attached to bone surfaces and readily available for homeostasis.[18] Apparently, the important effect of the drug is not due to mere removal of calcium.

It has been shown that edathamil increases the urinary excretion of certain trace metals. These trace metals form integral parts of many enzyme systems, and it seems that edathamil could remove trace metals from enzyme systems or bind competitive inhibiting metals. This effect through trace metals would be in accordance with the small quantities of cations affected.

The disappearance of clinical edema in one of our patients is noteworthy. Perhaps the apparent softening of the cutaneous

sclerosis was a result of the removal of water which might or might not have been clinically evident. This could explain also the improvement in function and esophageal motility.

Finally, it is possible that the effect of edathamil resulted from something other than its chelating properties. We could have witnessed a nonspecific effect, perhaps from stress. It remains unexplained why only some of the patients were benefited.

Summary and Conclusions

The purpose of this project was to explore the effects of a new potent chelating agent, edathamil disodium (Disodium Versenate), in patients with scleroderma. Twenty-three patients with scleroderma of varying degrees (twenty with acrosclerosis, two with diffuse scleroderma, and one with widespread morphea) were given edathamil intravenously in courses extending over a three-week period. Nine patients showed improvement as measured by functional performance tests, esophageal motility studies, and over-all clinical evaluation.

In our experience, edathamil is a relatively safe drug to administer by intravenous drip. Some degree of renal irritation should be anticipated, although at the dosage schedules recommended by Foreman and associates [9] it should be infrequent.

At the present time, in the absence of any specific therapeutic agent in scleroderma, the use of edathamil in the systemic forms of scleroderma seems justified. The ultimate usefulness of this drug in the treatment of scleroderma awaits further evaluation.

Mayo Clinic.

REFERENCES

1. Klein, R., and Harris, S. B.: Treatment of Scleroderma, Sclerodactylia, and Calcinosis by Chelation (EDTA), Am. J. Med. 19:798-807 (Nov.) 1955.

2. Nick, J.; Contamin, F.; Harl, J. M., and Morin, P.: Sclérodactylie avec calcinose digitale et prérotulienne (syndrome de Thibierge-Weissenbach) précédée d'un syndrome de Raynaud: Résultats du traitement par un agent chélateur (sel sodique de l'EDTA), Bull. et mém. Soc. méd. hôp. Paris 73:169-173 (Feb. 1-15) 1957.

3. Thiers, H.; Colomb, D.; Fayolle, J.; Taine, B., and Moulin, G.: Action des chélateurs décalcifiants dans le traitement des états sclérocicatriciels, Bull. Soc. franç. dermat. et syph. 64:304-305 (June-July) 1957.

4. Rukavina, J. G.; Mendelson, C.; Price, J. M.; Brown, R. R., and Johnson, S. A. M.: Scleroderma (Acrosclerosis): I. Treatment of Three Cases of the Non-Calcific Variety by Chelation (EDTA), J. Invest. Dermat. 29:273-288 (Oct.) 1957.

5. Foreman, H., and Trujillo, T. T.: The Metabolism of C^{14} Labeled Ethylenediaminetetra-Acetic Acid in Human Beings, J. Lab. & Clin. Med. 43: 566-571 (April) 1954.

6. Popovici, A.; Geschickter, C. F.; Reinovsky, A., and Rubin, M.: Experimental Control of Serum Calcium Levels in Vivo, Proc. Soc. Exper. Biol. & Med. 74:415-417 (June) 1950.

7. Spencer, H.; Vankinscott, V.; Lewin, I., and Laszlo, D.: Removal of Calcium in Man by Ethylenediamine Tetra-Acetic Acid: A Metabolic Study, J. Clin. Invest. 31:1023-1027 (Dec.) 1952.

8. Perry, H. M., Jr., and Schroeder, H. A.: Lesions Resembling Vitamin B Complex Deficiency and the Urinary Loss of Zinc Produced by Ethylenediamine Tetra-Acetate, Am. J. Med. 22:168-172 (Jan.) 1957.

9. Foreman, H.; Finnegan, C., and Lushbaugh, C. C.: Nephrotoxic Hazard from Uncontrolled Edathamil Calcium-Disodium Therapy, J. A. M. A. 160:1042-1046 (March) 1956.

10. Dudley, H. R.; Ritchie, A. C.; Schilling, A., and Baker, W. H.: Pathologic Changes Associated with the Use of Sodium Ethylene Diamine Tetra-Acetate in the Treatment of Hypercalcemia: Report of 2 Cases with Autopsy Findings, New England J. Med. 252:331-337 (March) 1955.

11. Clarke, N. E.; Clarke, C. N., and Mosher, R. E.: Treatment of Angina Pectoris with Disodium Ethylene Diamine Tetraacetic Acid, Am. J. M. Sc. 232:654-666 (Dec.) 1956.

12. Holland, J. F.; Danielson, E., and Sahagian-Edwards, A.: Use of Ethylene Diamine Tetra Acetic Acid in Hypercalcemic Patients, Proc. Soc. Exper. Biol. & Med. 84:359-364 (Nov.) 1953.

13. Clarke, N. E.; Clarke, C. N., and Mosher, R. E.: The "in Vivo" Dissolution of Metastatic Calcium, Am. J. M. Sc. 229:142-149 (Feb.) 1955.

14. Spencer, H.; Greenberg, J.; Berger, E.; Perrone, M., and Laszlo, D.: Studies on the Effect of Ethylenediaminetetraacetic Acid in Hypercalcemia, J. Lab. & Clin. Med. 47:29-41 (Jan.) 1956.

15. Peters, H. A.; Woods, S.; Eichman, P. L., and Reese, H. H.: The Treatment of Acute Porphyria with Chelating Agents: A Report of 21 Cases, Ann. Int. Med. 47:889-899 (Nov.) 1957.

16. Creamer, B.; Andersen, H. A., and Code, C. F.: Esophageal Motility in Patients with

Scleroderma and Related Diseases, Gastroenterologia 86:763-775, 1956.

17. Muller, S. A.: Scleroderma: The Relationship of Calcinosis and the Effects of a New Chelating Agent, EDTA, Thesis, University of Minnesota, Graduate School, 1958.

18. Howard, J. E.: Normal Calcium and Phosphorous Transport and Body Fluid Homeostasis, in Reifenstein, E. C., Jr., Editor: Conference on Metabolic Interrelations with Special Reference to Calcium, New York, Josiah Macy, Jr., Foundation, 1953, pp. 11-42.

Idiopathic Atrophoderma of Pasini and Pierini Occurring in Two Brothers

MARC ALLEN WEINER, M.D., and JAMES Q. GANT Jr., M.D., Washington, D. C.

Two brothers with identical bizarre eruptions were recently seen. Their dermatosis was of a type we had never before encountered. Fortunately, however, we had recently read the article by Orlando Canizares et al., "Idiopathic Atrophoderma of Pasini and Pierini."[1] According to their detailed and excellent description, there could be no doubt that these patients' lesions were examples of that entity.

Since the above-mentioned article is the only one by that name in the English-language dermatological literature, and since this condition has never been described in more than one member of a family, it was felt that this report might add a modicum of information about this unfamiliar dermatosis.

Two brothers, aged 17 and 19, respectively, presented themselves on April 1, 1958. They were both natives of the United States, of Italian parentage. The chief complaint was "brown patches on the trunk." Their parents, 15-year-old brother, and 13-year-old sister were free of any eruption.

Report of Cases

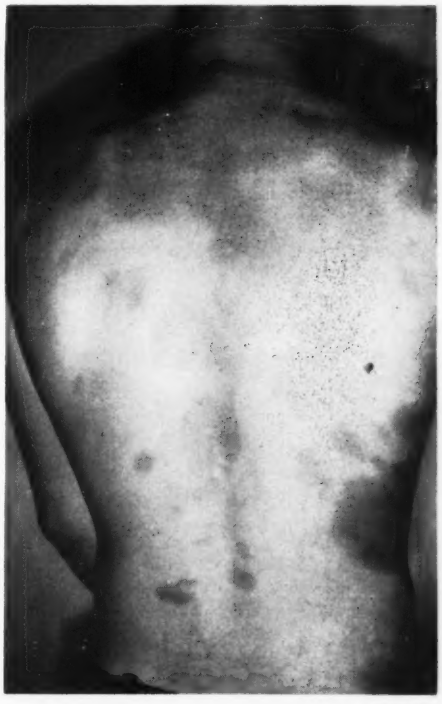
CASE 1.—Onset in the 17-year-old youth was three years previously, when an asymptomatic brown spot appeared on the left lateral chest. Since that time, numerous such small and large patches have appeared all over the torso and proximal arms. His general health has remained good.

Examination.—Over much of the torso and deltoid regions there are discrete, pea- to palm-sized, brown patches, most of which are slightly sunken below the skin level. The margins are distinct and beveled. There is no evidence of erythema, lilac border, induration, or sclerosis. In many of the patches the underlying veins are fuzzily visible. The surface of each patch is smooth and of apparently normal texture. The only exception to the above description is seen on the right lateral iliac crest region, where three lesions exhibit central whiteness and mild sclerosis. These latter changes developed within preexisting typical patches at some unknown later time (Figs. 1 and 2).

CASE 2.—Onset of the dermatosis in the 19-year-old youth was two years previously, in the left scapular region. As it slowly and asymptomatically enlarged, another patch appeared on the right lower back and another on the right forearm.

Examination.—On the left upper back there is a palm-sized patch of light-brown pigmentation. A similar smaller patch is present on the right lumbar region and another on the right volar forearm.

Fig. 1 (Case 1).—The back is profusely involved with small and large brown patches, most of which are slightly depressed below the surface.



Submitted for publication Dec. 19, 1958.

Figure 2

Fig. 2 (Case 1).—The right lateral view also reveals the beveled edges of the brown depressed patches. Note the three lesions on the crest of the ilium, which show central whiteness and mild sclerosis.

Figure 3

Fig. 3 (Case 2).—The atrophic patches on the left upper back and right lower back are light brown and do not photograph well in a swarthy person. In the original Kodachrome picture the underlying veins were fuzzily visible.

Mild depression of each patch is both visible and palpable. There is blurred visibility of the underlying veins. The surface of each patch is flat, soft, and smooth. The wide-spread folliculitis of the back spares these patches, although lanugo hair growth is undisturbed (Fig. 3).

Biopsy Findings

A punch biopsy was performed on the left upper back of each patient and was submitted to the Armed Forces Institute of Pathology. Dr. Elson B. Helwig described the histopathology as follows:

"The sections from both lesions appear essentially similar. The sections of tissue were examined by the following methods: hematoxylin and eosin, Snook's reticulum, Weigert's elastic, periodic acid-Schiff and acid mucopolysaccharide. The epidermis does not appear unusual and is of average thickness. The basal layer is distinctly pigmented. The capillaries of the upper corium are dilated but there is no swelling of the endothelial cells. In a few instances the capillaries are surrounded by lymphocytes. The collagen of the corium does not appear unusual and there is no abnormal disposition of PAS staining material nor of acid mucopolysaccharides. The elastic tissue is relatively abundant, in places appears coarse and especially in the deeper corium, occasionally clumped. The hair follicles, sebaceous glands and sweat glands are not unusual. The changes are interpreted as chronic dermatitis but are consistent with those noted in some of the reported examples of idiopathic atrophoderma."

Comment

The question as to whether or not idiopathic atrophoderma is a stage or variety of morphea will not be discussed here. This aspect has been fully covered in the article by Canizares et al. Suffice it to say that our patients conform to their description of the disease clinically, and, presumably, histopathologically ("presumably," because the

histopathology is variable and nonspecific at best).

We wish to add some clinical observations on our two patients which have either not been previously described or only superficially mentioned:

1. *Pinching of Skin.*—This is more difficult to do with the affected skin than with the adjacent normal skin and is attributed to the decreased thickness of the former.

2. *Elasticity of Skin.*—There is normal rebound of the affected skin. A curious phenomenon, however, was noted during the punch biopsy procedure. As the punch entered the dermis, the tissue plug began to shrink, and this continued to the full depth of penetration (to the fat). Some shrinkage is a normal occurrence, but we have never observed it to the extent that this tissue demonstrated it. The 5 mm. punch produced a plug of 3 mm. diameter; the 6 mm. punch, a plug of 4 mm. Is this due to decreased tissue substance (collagen), or to the action of normal (or stronger than normal) elastic tissue acting on decreased amount of tissue substance? The "usual" appearance of the collagen in our sections must be considered as somewhat artifactual since there was more than average shrinkage of the tissue. In vivo, the collagen bundles must have been more widely separated.

3. *Hair Growth.*—This is unaffected. The site of each hair follicle is distinctly visible by virtue of its being less pigmented than the affected surrounding skin but still flush with the surface.

4. *Follicular Keratoses.*—The older brother has a diffuse, slightly erythematous keratosis pilaris over most of the back. This alteration is not present in the atrophic patches.

5. *Erythema Production.*—When the skin is rubbed, erythema appears promptly in both the normal and the affected skin but appears more quickly and is more sustained in some of the atrophic patches.

6. *Blood Vessels.*—Underlying veins, as already noted, are visible as through ground glass in many of the atrophic patches. In addition, tiny capillaries and capillary loops (not of the order of telangiectases) are barely visible to the naked eye. They are very apparent, however, with a loupe ($\times$ 2¾ magnification), especially after rubbing the affected skin and applying a thin film of cedar oil.

7. *Sensation.*—There is normal sensitivity to touch and pin prick in the atrophic skin.

8. *Hypertrophic Scar Formation.*—Six weeks after biopsy excision was done, each patient exhibited an erythematous hypertrophic scar at the operative site. It struck us as odd that a deficient corium should react in this manner (endocrine factor?).

This form of idiopathic atrophoderma will undoubtedly be readily recognized since it has been introduced into the North American literature, but it is still unquestionably a rare condition. Its etiology is unknown, and the possibility of hereditary transmission has never had any support. The occurrence in two members of one family of a rare dermatosis, therefore, raises this possibility. A much larger number of case reports may shed some light on this factor.

Unfortunately, special stains (Snook's reticulum, periodic acid Schiff, and acid mucopolysaccharide) revealed no characteristic changes in the tissue sections.

Summary

The history and physical findings of two patients with idiopathic atrophoderma of Pasini and Pierini are described.

The fact of its occurrence in two brothers raises the possibility of hereditary transmission.

Some clinical observations not hitherto mentioned are described.

915 19th St., N. W.

REFERENCE

1. Canizares, O.; Sachs, P.; Jaimovich, L., and Torres, V.: Idiopathic Atrophoderma of Pasini and Pierini, A. M. A. Arch. Dermat. 77:42 (Jan.) 1958.

Dexamethasone in Dermatology

NORMAN B. KANOF, M.D., and SAUL BLAU, M.D., New York

Dexamethasone is 9-α-fluoro,16-α-methylprednisolone.* It is one of a group of prednisolone analogues synthesized and studied by Arth and his co-workers [1,2] in the continuing search for modifications of hydrocortisone which would afford increased anti-inflammatory and antiallergic activity but would produce minimal mineral imbalance and the other undesirable side-effects that sometimes result from therapy with the corticosteroids.

The formation of prednisone and prednisolone from cortisone and hydrocortisone by the introduction of a double bond (Δ-1) in the C_1-C_2 position increases the anti-inflammatory potency of hydrocortisone four or five times without enhancing its effect on sodium-potassium balance. Fluorination of hydrocortisone at the 9-α position increases its anti-inflammatory effect tenfold. However, the profound sodium-retaining and potassium-excreting effects of this modification interdicted its systemic use. Addition of a hydroxyl group in the 16-α position made it possible to utilize the enhanced anti-inflammatory and antiallergic activity of 9-α fluorination by eliminating the excessive effect on body electrolytes (triamcinolone). The screening studies conducted by Arth and his collaborators [1,2] indicated that the introduction of a methyl group at the 16-α position still further increased the anti-inflammatory activity of the steroid. They found that dexamethasone was 190 times more potent than hydrocortisone when measured by the granuloma-inhibition test yet did not produce electrolyte imbalance.

Boland [3] and Bunim et al.[4] have studied dexamethasone in the treatment of rheumatoid arthritis. Both authors found dexamethasone produced no sodium retention and had greater antirheumatic activity, milligram for milligram, than previously studied corticosteroids. However, increased anti-inflam-

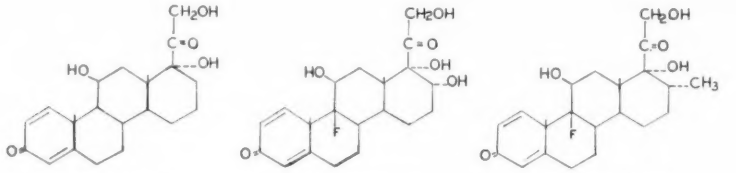


TABLE 1.—*Dermatoses Treated with Dexamethasone*

	No.
Atopic dermatitis	17
Psoriasis	7
Eczematous dermatitis	6
Urticaria	5
Contact dermatitis	4
Alopecia totalis	1
Lichen planus	2
Erythema multiforme	1
Dermatitis herpetiformis	1
Nummular eczema	2
Generalized erythroderma	1
Total	47

Submitted for publication Jan. 14, 1959.

From the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School (Dr. Marion B. Sulzberger, Chairman) and the Skin and Cancer Unit of the New York University Hospital.

* The dexamethasone used in this study was supplied as Decadron by Merck Sharp & Dohme, Westpoint, Pa.

matory activity is not synonymous with therapeutic superiority. Increased dissociation of the anti-inflammatory and antiallergic effects from unwanted side-effects is the essential criterion for a "better" corticosteroid. Much further investigation is necessary to evaluate dexamethasone properly. We wish to present our experiences with this steroid in the treatment of various dermatoses.

Method

Forty-seven patients from private practice were treated with dexamethasone by mouth. All patients

TABLE 2.—*Effects of Dexamethasone*

				Dexamethasone						
				Duration Treatm.,	Dose, Mg.			Prev. Steroid Dose, Mg.		
No.	Age	Sex	Diagnosis	Wk.	Initial	Maint.	Side-Effects	Steroid *	Initial	Maint.
1	33	F	Atopic dermatitis	13	3.2	1.6	+5 lb.; acne	T	16	8
2	37	M	Atopic dermatitis	4	4.8	—	Epigastric distress	P	40	20
3	33	F	Psoriasis	14	4.0	2.4	+4 lb.; bloating	T	24	12
4	40	F	Atopic dermatitis	18	3.2	1.6	—	T	16	10
5	29	M	Urticaria	15	3.2	2.4	+11 lb.; acne	P	40	30
6	23	M	Alopecia totalis	24	3.2	1.5	+8 lb.; moon facies	—	—	—
7	47	M	Atopic dermatitis	16	3.2	1.2	+6 lb.; jittery	P	30	15
8	55	F	Lichen planus	8	3.0	—	—	—	—	—
9	21	F	Atopic dermatitis	14	3.2	0.5	+5 lb.; increased appet.	—	—	—
10	40	F	Eczematous dermatitis	12	4.8	1.0	—	—	—	—
11	31	M	Erythema multiforme	6	3.0	—	—	—	—	—
12	10	M	Atopic dermatitis	12	2.4	1.0	—	—	—	—
13	21	F	Contact dermatitis	16	3.2	1.6	+6 lb.	—	—	—
14	28	F	Psoriasis	12	3.2	2.0	Gastrointestinal upset	—	—	—
15	27	F	Urticaria	7	4.0	2.0	—	—	—	—
16	50	M	Eczematous dermatitis	11	4.8	1.6	—	—	—	—
17	10	F	Atopic dermatitis	9	3.2	2.0	—	—	—	—
18	56	M	Nummular eczema	4	2.4	—	—	—	—	—
19	51	F	Dermatitis herpetiformis	20	3.2	1.2	+12 lb.; bloating; jittery	T	16	6
20	37	M	Lichen planus	8	4.0	1.5	—	—	—	—
21	23	F	Atopic dermatitis	17	1.6	1.2	+7 lb.; increased appet.	—	—	—
22	44	F	Contact dermatitis	4	2.4	1.6	Jittery; insomnia	T	16	8
23	49	F	Contact dermatitis	4	3.2	—	—	—	—	—
24	42	M	Eczematous dermatitis	4	4.0	—	—	—	—	—
25	59	M	Psoriasis	12	3.2	2.0	+5 lb.; bloating; moon facies	T	16	10
26	57	F	Eczematous dermatitis	8	3.2	1.5	+15 lb.; weakness	—	—	—
27	60	F	Psoriasis	10	6.0	3.0	—	—	—	—
28	27	F	Atopic dermatitis	21	3.2	2.0	+11 lb.; bloating	T	16	8
29	52	M	Atopic dermatitis	11	4.0	3.2	+16 lb.; increased appet.; jittery	T	24	10
30	18	F	Atopic dermatitis	16	1.6	1.5	+11 lb.	T	16	6
31	26	F	Urticaria	5	6.0	—	—	—	—	—
32	34	F	Eczematous dermatitis	14	3.2	2.0	+5 lb.; moon facies	T	24	16
33	43	F	Eczematous dermatitis	8	5.0	2.0	—	—	—	—
34	38	M	Nummular eczema	6	6.0	1.5	—	—	—	—
35	34	M	Atopic dermatitis	16	3.2	2.4	+11 lb.; increased appet.; jittery, insomnia	T	24	16
36	37	M	Atopic dermatitis	22	1.6	1.0	—	P	20	10
37	44	F	Psoriasis	16	4.0	2.0	—	—	—	—
38	49	M	Psoriasis	9	4.0	2.5	—	—	—	—
39	30	F	Urticaria	6	4.0	1.5	—	—	—	—
40	38	F	Atopic dermatitis	8	1.6	1.2	+10 lb.; bloating; moon facies	—	—	—
41	27	M	Contact dermatitis	4	4.0	—	—	—	—	—
42	31	M	Urticaria	6	5.0	2.0	—	—	—	—
43	43	F	Psoriasis	13	3.0	1.5	—	—	—	—
44	37	M	Atopic dermatitis	17	3.2	2.5	+7 lb.	—	—	—
45	36	F	Atopic dermatitis	7	3.2	2.4	Acne	—	—	—
46	66	M	Generalized erythroderma	5	4.0	1.5	—	T	24	16
47	27	F	Atopic dermatitis	5	4.0	1.5	—	—	—	—

* P indicates prednisolone; T, triamcinolone.

were ambulatory. Their ages ranged from 10 to 66 years. Twenty-seven were females, and twenty were males. Most of these patients had widespread eruptions with a marked inflammatory component and intense pruritus. Many had been treated with other corticosteroids.

At the beginning of this study, dexamethasone was supplied in 0.4 mg. tablets. Later, the tablet size was changed to 0.5 mg. The daily amount was taken in four doses. The initial suppressive dose ranged from 1.6-6.0 mg. daily (average, 3.0-4.0 mg.) depending on the nature and severity of the dermatosis. When marked clinical improvement was achieved, the amount of the drug was slowly reduced to determine a maintenance level. This ranged from 0.4-3.0 mg. (average, 1.6-2.0 mg.). Patients were observed each week during the initial suppressive phase of therapy and at a one- or two-week interval thereafter. There were no dietary restrictions or supplements. These patients were maintained on uninterrupted therapy with dexamethasone for 4 to 24 weeks (Table 1).

Results

Dexamethasone has potent anti-inflammatory and antiallergic activity in the treatment of various dermatoses. Seventeen patients with atopic dermatitis, seven patients with psoriasis, and five patients with urticaria showed marked improvement. Contact dermatitis, lichen planus, nummular eczema, erythema multiforme, dermatitis herpetiformis, eczematous dermatitis, and generalized erythroderma also responded to therapy with dexamethasone. Regrowth of hair in alopecia totalis was initiated and maintained with dexamethasone. The effective therapeutic dose will vary with the dermatosis. An initial daily dose of 3.0-5.0 mg. will usually produce a good improvement within a week. A lower maintenance dose can then be established.

In those patients who had been treated with other corticosteroids, the effective dose of dexamethasone, milligram for milligram, was one-fourth to one-eighth that of triamcinolone and up to one-tenth that of prednisolone (Table 2).

Side-Effects

Effective therapeutic doses of dexamethasone, despite the small amounts required, frequently produced annoying side-effects.

TABLE 3.—*Side-Effects from Dexamethasone*

	No.
Weight gain	18
Bloating	5
Acne	3
Jittery, insomnia	5
Gastrointestinal upset	2
Moon facies	4

Eighteen patients gained weight while taking dexamethasone. The increase ranged from 4 to 16 lb. and was usually associated with increased appetite and caloric intake. Five patients complained of "bloating," and four showed moon facies and buffalo hump. No patients presented weight loss or muscle wasting. Three patients developed an acneiform eruption while taking dexamethasone, and two complained of mild gastrointestinal symptoms. Five patients were stimulated and "jittery" while taking the drug and felt that it caused insomnia. No patient in this series developed glycosuria. All of these side-effects disappeared when the drug was stopped (Table 3).

Summary and Conclusions

Dexamethasone by mouth was found to have marked anti-inflammatory, antipruritic, and antiallergic effects in 47 patients with various dermatoses treated for 4 to 24 weeks.

The initial daily dose of dexamethasone required for suppression of these dermatoses ranged from 3.0-5.0 mg. The average maintenance dose was 1.6-2.0 mg. daily.

Side-effects are encountered with therapeutically effective doses of dexamethasone. Weight gain, "bloating," and extreme nervousness were the most annoying effects.

580 5th Ave.

REFERENCES

1. Arth, G. E.; Johnston, D. B. R.; Fried, J.: Spooncer, W. W.; Hoff, D. R., and Sarett, L. H.: 16-Methylated Steroids: I. 16-Alpha Methylated Analogs of Cortisone; A New Group of Anti-Inflammatory Steroids, J. Am. Chem. Soc. 80: 3160, 1958.

2. Arth, G. E.; Fried, J.; Johnston, D. B. R.; Hoff, D. R.; Sarett, L. H.; Silber, R. H.; Stoerk, H. C., and Winter, C. A.: 16-Methylated Steroids: II. 16-Alpha Methyl Analogs of Cortisone; a New Group of Anti-Inflammatory Steroids; 9-Alpha Halo Derivatives, J. Am. Chem. Soc. 80:3161, 1958.

3. Boland, E. W.: 16-Alpha Methyl Corticosteroids, Col. Med. 88:417, 1958.

4. Bunim, J. J.; Black, R. L.; Lutwak, L.; Peterson, R. E., and Whedon, G. D.: Studies on Dexamethasone: A New Synthetic Steroid in Rheumatoid Arthritis; a Preliminary Report, Arthritis & Rheumat. 1:313, 1958.

Ringworm of the Scalp in the Delta of the Rio Grande

IVAN W. KUHL, M.D., McAllen, Texas

The presence of tinea capitis in abundance in the semitropical delta of the Rio Grande river has considerable geomedical implications.

The permanent population of "The Valley" consists primarily of native Texans of Mexican descent and transplanted Midwesterners. There is also a liberal sprinkling of natives of Mexico and native Texans of European descent, particularly German and Scotch-Irish. Negroes form less than 1% of the population. It is estimated that 50%-60% of the population is of Mexican descent.

It also has other transient population of special note in the form of two Air Force bases, numerous border patrolmen, considerable oil and gas activity—with its transient crews and families, and a burgeoning tourist trade. The latter, however, at present, is composed chiefly of senior citizens who have little contact with the permanent residents, being seasonally congregated in tourist facilities for the most part.

This area is the largest of three populous essentially agricultural areas on the Mexican border and is, therefore, a mainstream for unskilled and semiskilled Mexican immigration. In the past it was the wetback's (and his family's) favorite entry area. At the present, it is a great user of bracero labor for its winter vegetables and citrus crops and summer cotton picking. The winter vegetable and citrus care and harvest provide the migrant workers with work in a warm climate which the Latin prefers by nature.

The mechanization of American farms and the shift of the population from rural to urban in predominance has left seasonal "vacuums" in unskilled and semiskilled labor for our rural areas. This demand has been met by seasonal importation of labor from many areas—the West Indies, Mexico (bracero), the South (Negro), and the Southwest (Latin-American). Those laborers imported from outside the United States are screened by the Immigration Service, but domestic migration is unscreened.

The seasonal migration of Latin-American workers from "The Valley" has been occurring for the past half century. It was instigated by the recruiters of sugar beet companies for cultivation and harvest of their crops. The mechanization of sugar beet harvesting in the past 10 years has decreased the demand for this labor, so the migrants have sought to sell their services in the groves, orchards, cotton, and vegetable fields of the West, Midwest and South. The official figures of the Texas Employment Commission in 1956 [1] and 1957 [2] showed these workers went to 35 states, including all except New England, New York, New Jersey, Pennsylvania, West Virginia, North Carolina, Nevada, Maryland, and Alaska.

Submitted for publication Dec. 19, 1958.

TABLE 1.—*Sex and Type Incidence of Cases of Tinea Capitis*

Sex	Totals	T. Tonsurans	M. Canis	T. Violaceum	T. Gypseum	M. Fulvum
M	136	95	39	3	0	0
F	135	108	20	5	1	1
Totals	271	203	59	8	1	1

The size of the out-of-state migration is not tremendous but is impressive. The Texas Employment Commission estimates that these figures comprise 75% of the migration from "The Valley" area. In 1956, 734 crews were registered, consisting of 17,282 people, of which 5,368 were nonworkers (children primarily). In 1957, 1,018 crews consisting of 24,331 people (7,778 nonworkers) were registered. The internal (follow the cotton picking) Texas migration amounted to 18,782 workers in 1956 and 14,397 workers in 1957.

In addition to these "homing pigeons," a considerable number of these Latins over the years stayed in northern states. They may act as foci of infection or as temporary foci when they act as hosts for their transient cousins.

Experience

For two years cultures were done on every case of tinea capitis seen in my office, and the results are herein reported. Only cases grown successfully are tabulated.

In this time, 271 patients having tinea capitis with positive cultures were seen. One patient who had Microsporum canis and Trichophyton-tonsurans simultaneously appears as two cases.

There was one case of M. canis infection in a 27-year-old Latin woman, but all other adult cases were T. tonsurans.

Comment

The mature age group was entirely feminine. Women usually have closer and more persistent natural familial contact with juveniles than their masculine counterparts. This (feminine preponderance) incidentally, agrees with Pipkin's[3] figures. It also is interesting to note that of these adult cases six refused treatment, despite the fact that some were found on contact investigation as likely sources for juvenile cases in their own families.

Because of the distribution to include all age groups (to age 70 in this series) and the long potential duration (30 years longest here), T. tonsurans is particularly prone to become widely distributed geographically. Its benign nature in the cases of long duration makes it only slightly bothersome; therefore a person may be an unsuspected carrier for many years.

Although the tinea cases were preponderantly Latin-American (79%—215 cases) and the T. tonsurans cases were more preponderantly Latin (85%—173 cases), I feel this difference does not represent a specific susceptibility. The difference can be explained on the basis of exposure because of economic and socioeconomic factors.

The general trend of northward decreasing preponderance of T. tonsurans[4] from Gonzalez Ochoa's 89.4% (in Mexico City) through the Valley's 75%, Pipkin's 20.6% (San Antonio), Seale's 20.6% (Houston), to Indianapolis' 2.2%, tends to confirm Pipkin's thesis that the infection is an invader from Mexico. Cases have been reported from many of the states being "invaded" by our Latin migratory workers—and will continue to be seen, I am sure.

TABLE 2.—*Age and Sex Incidence of Cases of T.-Tonsurans Infection of the Scalp*

	Age, Yr.			
	0-5	6-11	12-20	20+
M	42	44	9	0
F	39	53	6	10
Totals	81	97	15	10

Summary

This paper confirms Pipkin's designation of south Texas as an endemic area of T. tonsurans scalp infections (75%) and outlines the mechanics of its principal mode of spread from this endemic area. It is written to emphasize the necessity for dermatologists in the United States to maintain a high index of suspicion for this resistant and deceptive type of tinea capitis.

414½ S. Main.

REFERENCES

1. LeBlanc, H.: Interstate Crews in Local Office Areas—1956: Interoffice Memorandum, Farm Placement Department, Texas Employment Commission, March 5, 1957.

2. LeBlanc, H.: Interstate Crews in Local Office Areas—1957: Interoffice Memorandum, Farm Placement Department, Texas Employment Commission, March 21, 1958.

3. Pipkin, J. L.: Tinea Capitis in the Adult and Adolescent, A. M. A. Arch. Dermat. & Syph. 66:9-36 (July) 1952.

4. Pinkerton, M. E.; Mullins, J. F., and Shapiro, E. M.: The Ecology of Superficial Fungus Infection in Galveston, Texas: A 5-Year Survey, Texas Rep. Biol. & Med. 15:26-49 (Spring) 1957.

Erythromycin in the Treatment of Early Syphilis

A Preliminary Report

C. HUNTER MONTGOMERY, M.D., and JOHN M. KNOX, M.D., Houston, Texas

In 1953, Keller and Morton [1] first reported on the treponemicidal properties of erythromycin in vitro, utilizing a variety of treponemal strains. They reported cultivatable treponema to be very susceptible to the action of erythromycin. The following year, Turner and Schaeffer [2] confirmed their report by comparing the effectiveness of various antibiotics in experimental rabbit syphilis. They found Treponema pallidum more sensitive to erythromycin and carbomycin than to any of the other antibiotics except penicillin and suggested further therapeutic trials. On the other hand, Kolmer [3] in a similar comparative study reported both oxytetracycline and tetracycline superior to erythromycin in treponemicidal properties.

In 1954, Alexander and Schoch [4] reported on four patients with early syphilis treated with 200 mg. of oral erythromycin four times daily for eight days (total dose of 6.4 gm.). T. pallidum disappeared from the lesions in 24 to 30 hours, and healing occurred as promptly as was usual with any other therapeutic agent. More recently, Montero [5] presented 27 cases of early syphilis he had treated with erythromycin. Twenty-one cases received 400 mg. and five cases 300 mg. three times daily for 10 days (total doses of 9 and 12 gm.). Twenty of these patients were darkfield positive before treatment, and all became darkfield negative within four days. All cases were seropositive prior to therapy, and on observation that varied between two months and two years all became seronegative or showed reductions in titer.

While many of the newer antibiotics other than erythromycin have been found to possess antisyphilitic activity, carefully studied dosage schedules for these antibiotics have been relatively large by comparison with the previously cited erythromycin reports. Rodriguez et al.,[6] using a total dose of 70 gm. of chlortetracycline; Taggart et al.,[7] using approximately 30 gm. of either chlortetracycline or chloramphenicol, and Robinson,[8] using 48 gm. of oxytetracycline have all obtained good results in the treatment of early syphilis. More recently, Hookings and Graves [9] have evaluated carbomycin in a total dosage of 21 gm. given over a period of 10 days with equally good results. Most workers have recommended larger dosages for late symptomatic syphilis, especially cardiovascular and neurosyphilis. Dosages of this magnitude, while effective, have been very expensive in comparison with penicillin and nearly prohibitive for use in public health venereal disease clinics. Our present study was undertaken to evaluate further the use of relatively small total dosages of erythromycin in the treatment of early syphilis.

Method of Study

Forty darkfield-positive cases of early syphilis have been treated with a total dosage of 9 to 10 gm. of oral erythromycin stearate or 2 gm. of

Submitted for publication Nov. 5, 1958.

Supported in part by a grant from Abbott Laboratories, North Chicago, Ill.

Director, Venereal Disease Clinic, City Health Department (Dr. Montgomery); Associate Professor of Dermatology, Baylor University College of Medicine (Dr. Knox).

TABLE 1.—*Erythromycin in the Treatment of Early Syphilis* *

Patient	Diagnosis	Darkfield, Days								VDRL in Dilutions, Mo.										
		0	1	2	3	4	5	6	7	0	1	2	3	4	5	6	7	8	9	10
1	Primary	+	+						—	WR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
2	Primary	+			+	—	—			16	8	WR	WR	NR	NR	NR	NR	WR	WR	
3	Secondary	+	—			—				16	8		WR	WR	NR	NR	NR	NR		
4	Secondary	+	+	+	—	—				64	8	4	2		WR	WR	WR	NR		
5	Secondary	+	+	—						16		2		WR	WR	WR				
6	Secondary	+	+			—				128	64	32	16	16	8	16	32	-- Relapse --		
7	Primary	+	+	—	—					4	2	2	WR	NR	WR	WR				
8	Primary	+	—	—						8		8	NR	NR	NR					
9	Primary	+	+	—	—					4	8	4	2	2	1					
10	Secondary	+	—	—							32	8	4	4						
11	Secondary	+	+			—				64	16			2						
12	Secondary	+	—				—			32				WR						
13 †	Secondary	+								16	8 ‡	4	2	WR						
14	Secondary	+			—					64	8	2	2							
15	Primary	+	+		—					NR	NR	NR	NR							
16	Primary	+								NR	NR	NR	NR							
17	Primary	+								32		16	-- Relapse --							
18	Primary	+								64	8		WR							
19	Primary	+								NR			NR							
20 †	Secondary	+								32	2		WR							
21	Primary	+								16			4							

* Dosage: 250 mg. orally q. i. d. for 10 days. + indicates positive; —, neagtive; WR, weakly reactive; NR, nonreactive.

† Pregnant

‡ Received 10 gr. of tetracycline at time of abortion.

intramuscular erythromycin ethyl succinate.* The time dosage schedules employed were as follows:

250 mg. orally q. i. d. for 10 days,
500 mg. orally q. i. d. for 5 days,
750 mg. orally q. i. d. for 3 days,
200 mg. I. M. o. d. for 10 days.

When possible, darkfield examinations were done daily until negative on two consecutive days. Serum serologic tests were done monthly for one year. Spinal fluid cell counts and serologic tests were obtained at the end of a year's follow-up. All patients reported have had a minimum of three months' follow-up.

Results

The results of therapy with 1 gm. of erythromycin daily for 10 days are shown in Table 1. T. pallidum disappeared from lesions in 24 to 96 hours. Nineteen of the twenty-one patients have had reductions from their original VDRL titer or remained seronegative. There have been two treatment failures. One patient developed a second darkfield positive chancre at the site of his original lesion. The other patient had a serologic relapse five months after therapy. Average follow-up for the group has been five months. Two prepartal patients with secondary syphilis are included in Table 1. Patient 13 was four months pregnant when treatment was begun and after one month had a septic abortion of unknown cause. Pathologists were unable to establish a syphilitic etiology on examination of the fetus. She received 10 gm. of tetracycline over a seven-and-one-half day period at the time of abortion. Her serologic titer had begun to fall at the time of abortion, and she has failed to show evidence of relapse. The other patient, No. 20, was seven months pregnant when treatment was initiated. She had a normal, uncomplicated term delivery of a viable infant. Cord blood had a VDRL of 1:1 at the time of delivery, but the child showed no evidence of congenital syphilis, and this probably represents only passive transfer of reagin from the mother. The infant will be reevaluated at three months of age.

* Supplied as Erythrocin and Erythrocin I. M. by Abbott Laboratories, North Chicago, Ill.

TABLE 2.—*Erythromycin in the Treatment of Early Syphilis**

Patient	Diagnosis	Darkfield, Days							VDRL in Dilutions, Mo.												
		0	1	2	3	4	5	6	7	0	1	2	3	4	5	6	7	8	9	10	11	12	LP
22	Primary	+	−	−						WR	WR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
23	Secondary	+	+			−				1	2	WR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
24	Primary	+	−	−						2	2	NR	NR			NR	NR	WR		64	Probable reinfection		
25	Primary	+			−					16	2		NR	NR	NR	NR	NR		NR				
26	Primary	+		−						64		16	4			4	2						
27	Primary	+	+	−				−		4	2	WR	WR	WR	WR	NR							
28	Primary	+	+	−	−					4			NR	4 -- Relapse --									
29	Primary	+		−	−					WR	WR	NR	NR										
30	Secondary	+								64	32	16	64 -- Relapse --										
31	Primary	+		+			−		−	4	2	WR -- Relapse --											

* Dosage: 500 mg. orally q. i. d. for 5 days. + indicates positive; −, negative; WR, weakly reactive; NR, nonreactive.

TABLE 3.—*Erythromycin in the Treatment of Early Syphilis* *

		Darkfield, Days								VDRL in Dilutions Mo.								
Patient	Diagnosis	0	1	2	3	4	5	6	7	0	1	2	3	4	5	6	7	8
32	Primary	+			—					NR	NR	NR	NR	NR		NR		NR
33	Secondary	+	+	—						64	16	8	8	16	32	Relapse		
34	Secondary	+	+	—	—					64	32		4	8	16	Relapse		
35	Primary	+	+						—	2			4			Relapse		
36	Primary	+			+					64			32			Relapse		
37	Primary	+		—						64	16	64				Relapse		
38	Primary	+	—							NR		16	Relapse or reinfection					

* Dosage: 750 mg. orally q. i. d. for 3 days. + indicates positive; —, negative; WR, weakly reactive; NR, nonreactive.

The follow-up on patients treated with 2 gm. of erythromycin daily for five days is shown in Table 2. The disappearance time of spirochetes varied from 24 to 76 hours; however, only 1 patient was still darkfield positive at 48 hours. All were seropositive at the onset of therapy, and five have now attained seronegativity. There have been four treatment failures. One of these failures occurred eight months after therapy, was preceded by six months of seronegativity, and in all likelihood represents a reinfection. Two patients have completed a year's follow-up, at which time cerebrospinal fluid examination revealed normal cell counts and nonreactive Kolmer complement-fixation tests. The average follow-up on this dosage schedule has been seven months.

The results of treatment with 3 gm. of erythromycin daily for three days are shown in Table 3. Darkfield negativity was attained by 48 hours with the exception of one patient, who was positive at 72 hours. Six of the seven patients have been retreated; three for a serologic relapse and three for recurrent darkfield positive lesions. The husband of one of the patients was completely uncooperative, refusing either examination or treatment in our clinic or by a private physician. Therefore, it is possible that she represents reinfection or relapse. Only one seronegative primary patient has failed to show evidence of relapse after eight months.

The results of therapy in two patients treated with 200 mg. of erythromycin intramuscularly daily for 10 days are shown in Table 4. Darkfield examinations were negative within 48 hours after the onset of therapy. One of these patients has attained seronegativity, and the other has had a reduction in titer and has shown no evidence of relapse. Both of these patients have a five-month follow-up.

Comment

At this time, two patients on the oral 10-day treatment schedule have shown evidence of treatment failure. Numerous treatment failures have occurred on both of the shorter courses of therapy, even though the total dosages were comparable. This was not surprising, since, in 1946, Eagle et al.,[10] using penicillin in experimental rabbit syphilis, demonstrated that the longer the duration of therapy the smaller the total dosage of penicillin necessary for cure.

TABLE 4.—*Erythromycin in the Treatment of Early Syphilis* *

		Darkfield, Days								VDRL in Dilutions, Mo.					
Patient	Diagnosis	0	1	2	3	4	5	6	7	0	1	2	3	4	5
39	Primary	+	+	—	—					WR	NR	NR	NR	NR	NR
40	Secondary	+	—	—						64	16	8	4	4	2

* Dosage: 200 mg., I. M. o. d. for 10 days. + indicates positive; —, negative; WR, weakly reactive; NR, nonreactive.

Apparently, this same principle holds true for erythromycin.

On numerous occasions we encountered deviations from the prescribed drug schedules on the oral program. For this reason there has always been objection to the use of self-administered medications in the treatment of venereal disease. The good results obtained in two patients treated with intramuscular erythromycin have been encouraging in this regard.

Side-effects have been minimal in patients receiving the smaller daily dosages of erythromycin. The use of 3 gm. daily has been associated with nausea, abdominal cramps, and diarrhea. Whether the diarrhea was sufficient to have interfered with absorption of the drug is not known. Side-effects, however, never necessitated the interruption or discontinuance of the drug.

That relatively small dosages of erythromycin exert a definite antitreponemal effect has been demonstrated. To establish whether either the oral or the intramuscular 10-day dosage schedule represents adequate therapy for early syphilis will require continued evaluation. It seems obvious that the three- and five-day dosage schedules are not adequate and it is doubtful that any of the schedules employed will prove altogether effective. Schedules using larger total dosages of erythromycin are now being evaluated.

Summary

Erythromycin, 250 mg., orally q. i. d. for 10 days, in the treatment of early syphilis has resulted in two treatment failures in 21 patients followed a minimum of three months. Two patients on this schedule were pregnant, one of whom had an abortion of unknown etiology, while the other delivered an apparently uninfected child.

Erythromycin, 500 mg. orally q. i. d. for five days, resulted in treatment failures in 4 of the 10 patients.

Erythromycin, 750 mg. orally q. i. d. for three days, resulted in treatment failures in six of the seven patients.

Two patients treated with 200 mg. of erythromycin intramuscularly in single daily injections for 10 days have been followed five months without evidence of relapse or reinfection.

Dr. Marolyn M. Cowart, Dr. Thomas D. Swafford, Dr. Lawrence E. Lundgren, and the personnel of both the Houston Health Department Laboratory and the Venereal Disease Clinic cooperated in this study.

Venereal Disease Clinic.

REFERENCES

1. Keller, R., and Morton, H. E.: Susceptibilities of Kazan, Nichols, and Reiter Strains of Treponema and Pleuropneumonia-like Organisms to the Antibiotic Erythromycin (Ilotycin), Am. J. Syph. 37:379-382 (July) 1953.

2. Turner, T. B., and Schaeffer, K.: The Comparative Effect of Various Antibiotics in Experimental Syphilis, Am. J. Syph. 38:81-91 (March) 1954.

3. Kolmer, J. A.: A Comparative Study of Ten Antibiotic Compounds in the Treatment of Experimental Syphilis of Rabbits, Antibiotics Ann. pp. 592-595, 1955-1956.

4. Alexander, L. J., and Schoch, A. G.: Erythromycin in Venereal Diseases, Am. J. Syph. 38:107-109 (March) 1954.

5. Montero, O.: Evaluation of Erythromycin in Early Syphilis, presented at the First International Symposium on Venereal Diseases and the Treponematoses, Washington, D. C., May 28-June 1, 1956.

6. Rodriguez, J.; Weinstein, S., and Parkhurst, G. E.: Aureomycin and Its Effect in Early Syphilis, A. M. A. Arch. Dermat. & Syph. 66:59-64, (July) 1952.

7. Taggart, S. R.; Romansky, M. J., and Landman, G. S.: Treatment of Syphilis with Aureomycin and Chloromycetin, Am. J. Syph. 36:174-178 (March) 1952.

8. Robinson, H. M., and Robinson, H. M., Jr.: Terramycin in the Treatment of Syphilis, Am. J. Syph. 35:479-481 (Sept.) 1951.

9. Hookings, C. E., and Graves, L. M.: Results of Treatment of Syphilis with Carbomycin: A Follow-Up Study, Antibiotics Ann. pp. 217-222, 1955-1956.

10. Eagle, H.; Magnuson, H. J., and Fleischman, R.: Effect of Method of Administration on Therapeutic Efficacy of Sodium Penicillin in Experimental Syphilis, Bull. Johns Hopkins Hosp. 79: 168-189 (Aug.) 1946.

The Psoriatic Process

DAPHNE ANDERSON ROE, M.D., M.R.C.P., Wilmington, Del.

In 1893, Audry [1] postulated that defective epidermal keratinization or cornification was the essential pathological feature of psoriasis. This hypothesis, based on histological studies, has been amply justified by recent biochemical investigations. However, before entering into a discussion of these recent findings, it would be well to reiterate Flesch's definition of the processes involved in cornification or rather in the maturation of the human epidermis.[2] He has called the consolidation of fibrous keratin precursors *keratinization* and the decomposition of cellular proteins or the formation of nonkeratinous components, in the horny layer, *differentiation*. These terms will be used forthwith in this paper.

Concerning keratinization, it has been found that, in psoriasis, a fibrous protein can be extracted from the scales, which is similar or identical with tonofibrin, which has previously been isolated from normal cellular epidermis.[3] This protein appears to be a fibrous, keratin precursor, with no sulfur content. Electron microscopic studies gave evidence that it might be the protein forming the tonofilaments in the epidermal cells which were described by Selby.[4] The experiments, which will be discussed here, give further support to this theory. This fibrous protein cannot be extracted from callus, in which we presume that keratinization is complete.

In psoriatic *horny layers*, three major anomalies occur in the process of differentiation. There is an increase in water soluble proteins, a decrease in free amino acid content, and an increase in the amount of pentoses.[2,5] Of these soluble proteins, the most significant is a glycoprotein,* with a carbohydrate content of 4.5 mg. %. This protein contains sulfhydryl groups and the carbohydrate radical consists of a sulfated mucopolysaccharide, probably chondroitin sulfate.[3] In water extracts of psoriasis scales, this protein can be isolated together with a free sulfated mucopolysaccharide.[6]

The decrease in free amino acid content and polypeptide content of psoriatic scales, has been thought to be due to decreased aminopeptidase activity,[7] though more recent studies have not confirmed this.[8]

Both combined and free pentoses are greatly increased in psoriatic scales.[9] Deoxyribose is also elevated, and the assumption has been made that these findings reflect abnormal nuclear metabolism with increased production and incomplete decomposition of nuclear proteins. This idea is supported by the finding of nucleoprotein in psoriatic scale extracts.[3] Ultraviolet absorption studies of such extracts reveal a nucleoprotein content of approximately 5%.

Our aim has been to study the anomalies of keratinization and differentiation in psoriasis, not in scale extracts, but in the pathological epidermis itself. Keratinization has been studied by polarization optical methods; differentiation, by the affinity of glycoprotein and free mucopolysaccharide for certain dyes.

Submitted for publication Jan. 14, 1959.

From the Department of Pathology, Memorial Hospital.

This investigation was supported by a grant from the Permanent Science Fund of the American Academy of Arts and Sciences. The manuscript received a prize from the Research Aid Committee of the American Dermatological Association, Inc.

* In a recent single experiment, a glycoprotein, similar in chemical characteristics to that extracted from psoriatic scale, was isolated from synovial fluid from a case of psoriasis arthropathica. This glycoprotein was not found in samples of synovial fluid from a patient with rheumatoid arthritis.[38]

Methods and Materials

A. Polarization Microscopy.—In the investigations, a Reichert monocular microscope was used, fitted with polaroid disks as substage polarizer and tube analyzer. A Retina IIC camera with a Schneider Xenar coated F28 lens was attached for photographic records. The sign of birefringence was determined by means of a first-order red-retardation plate, used as described by Schmitt.[10]

Birefringence was referred to the optic axis of the component fibrous structure in the histological material under examination.[11]

The following specimens were examined using this equipment:

1. Unstained sections of callus and scales from cases of psoriasis and ichthyosiform erythroderma, cut perpendicular to the surface place
2. Whole mounts of callus and scales from cases of psoriasis and ichthyosiform erythroderma
3. Vertical sections of normal, hyperkeratotic, and psoriatic skin.

The scales and callus were fixed in 1% trichloracetic acid in 80% ethyl alcohol, embedded in paraffin and sectioned to 6μ thickness.

The sections were deparaffinized with xylene and mounted in synthetic resin.

The whole mounts were cleared with xylene and mounted in synthetic resin with the free surface uppermost.

The skin samples were fixed in 10% formalin and embedded in paraffin. Sections were cut to 3μ thickness, cleared, and mounted as described above.

B. Histochemistry.—The modification of the Gram-Weigert stain, used by Johnson et al.[12] in the demonstration of cat-tongue keratins was applied to the sections described above. A buffered thionine stain described by Lillie[13] was applied for the demonstration of metachromatic substances (Sections were stained for 30 minutes in 0.05% thionine in a 0.01 M acetate buffer).

The Alcian blue technique used by Goltz et al.[14] was followed in order that acid mucopolysaccharides might be distinguished. These three staining methods were used before and after incubation of the sections with testicular hyaluronidase (10 mg/100 ml. in a phosphate buffer at pH 6.5 for 60 minutes at 37 C). Barrnett and Seligman's dihydroxldinaphthyl disulfide method for sulfhydryl groups[15] was also utilized.

The Gram-Weigert stain, as applied in the staining of sections, was also used to investigate the dye affinity of samples of the fibrous protein and the glycoprotein isolated from extracts of psoriasis scales.

Results

A. Polarization Microscopy.—Psoriasis scale sections reveal a system of birefringent fibers, running perpendicular or at an angle to the surface plane (Fig. 1). These are fine fibers or fibrils which under high-power magnification can be seen to run tangentially to the nuclei in the parakeratotic cells or from the nucleus to the cell margins. In addition, there are scattered groups of wider, more intensely birefringent fibers, parallel to the surface plane (Fig. 2). Both types of fibers show a maximum brightness, with their longitudinal axes set at 45 degrees from the polarizing directions of the polarizer and analyzer. The sign of birefringence is positive in each case with respect to the longitudinal axis. The fibers running

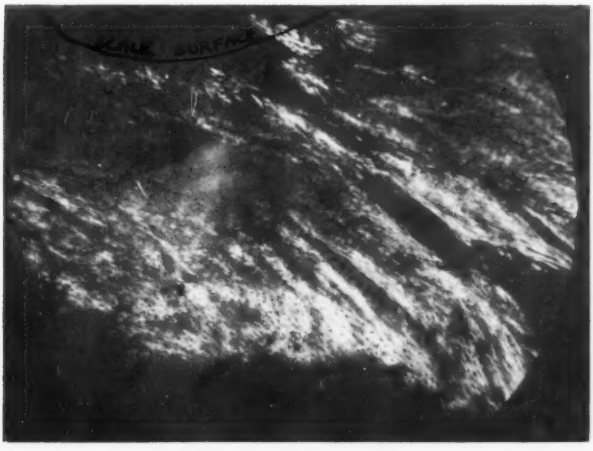


Fig. 1.—Vertical section of psoriatic scale, showing birefringent fibers running perpendicular or at an angle to the surface plane; × 200.

Fig. 2.—Vertical section of psoriatic scale, showing perpendicular birefringent fibers and groups of mature keratin fibers parallel to the surface plane; × 400.

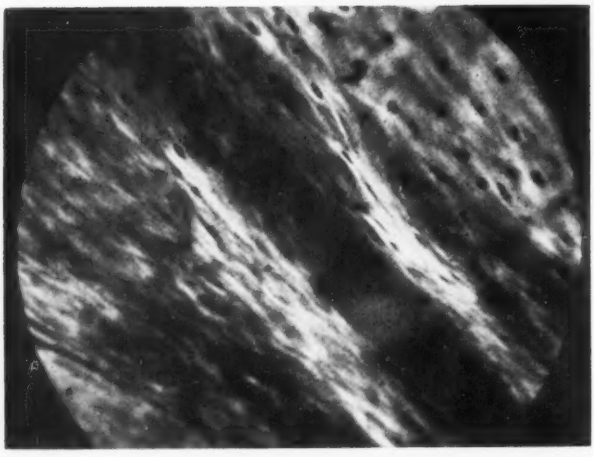


Fig. 3.—High-power magnification of section of psoriatic scale, showing birefringent tonofibrillar system of the parakeratotic cells with lateral aggregation of fibers in some areas; × 900.

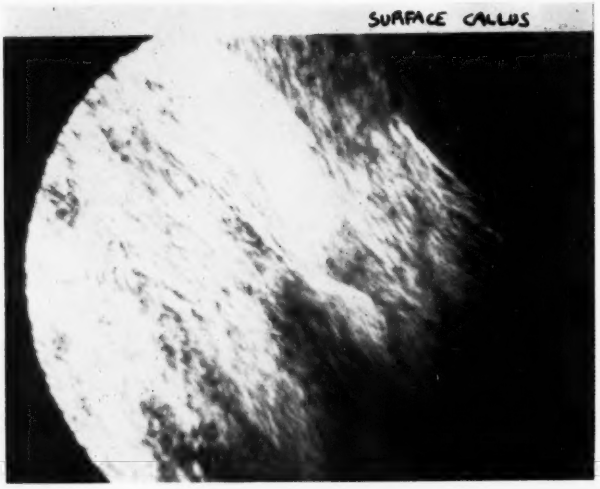


Fig. 4.—Vertical section of callus, showing mature keratin fibers, parallel to the surface plane, under polarized light; × 400.

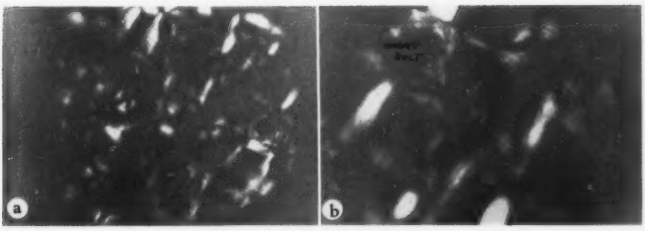


Fig. 5.—Whole mount of psoriatic scale. The birefringent fibers are perpendicular to the surface plane except where there are small groups of mature keratin fibers. Note the persistance of circularly oriented fibers around the opening of a sweat duct; Reduced 50% from mag. (*a*) × 200; (*b*) × 400.

through the parakeratotic cells closely resemble the birefringent fibrillar system of the normal cellular epidermis, though they are more numerous and packed together (Fig. 3). The parallel fibers resemble the normal doubly refractile fibers seen in callus (Fig. 4).

Whole mounts of psoriasis scale confirm these findings, showing that most of the hyperkeratotic epidermis from the sole of the foot. In these sections, too, the birefringent system of tonofibrils is seen very clearly, directed in the deeper layers of the stratum Malpighii, perpendicular to the surface and more superficially, at various angles to the surface. However, in general, the plane of orientation of the tonofibrils is at right angles to the fibers in the corneal

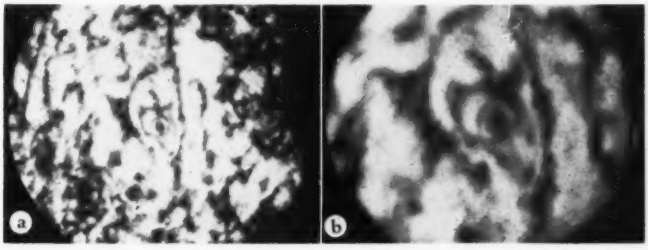


Fig. 6.—Whole mount of callus, showing birefringent fibers parallel to the surface, arranged in whorl pattern related to ridges and grooves. A sweat duct is prominent in the center of the field; reduced 45% from mag. (*a*) × 200; (*b*) × 400.

fibers are perpendicular to the surface plane and that the normal pattern of callus is lost, though the circularly oriented fibers round the sweat duct openings remain. In whole mounts of scales from ichthyosiform erythroderma and callus, the oriented fibers are parallel to the surface (Figs. 5-7).

The parallel and intense form of birefringence first appears in the keratogenous zone. This is best seen in sections of layer (Fig. 8). These latter findings confirm earlier observations.[16,17] This pattern is not followed in the psoriatic epidermis. Here, the tonofibrils appear to be reduced in number or else they are not sufficiently oriented to show anisotropy. This tonofibrillar system reaches the surface of the psoriatic epidermis in many areas. Near the surface, the fibrils are clumped and their angle to the surface plane is reduced. The

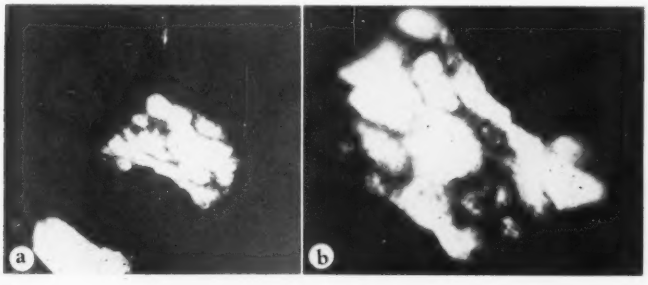


Fig. 7.—Whole mount of scale from ichthyosiform erythroderma, showing similar pattern of birefringent fibers to that seen in callus; reduced 35% from mag. (*a*) × 200; (*b*) × 400.

Fig. 8.—Vertical section of hyperkeratotic epidermis, showing birefringent keratin fibers in corneal layer and tonofibrillar system of the Malpighian layer, the latter mainly perpendicular to the surface plane; × 200.

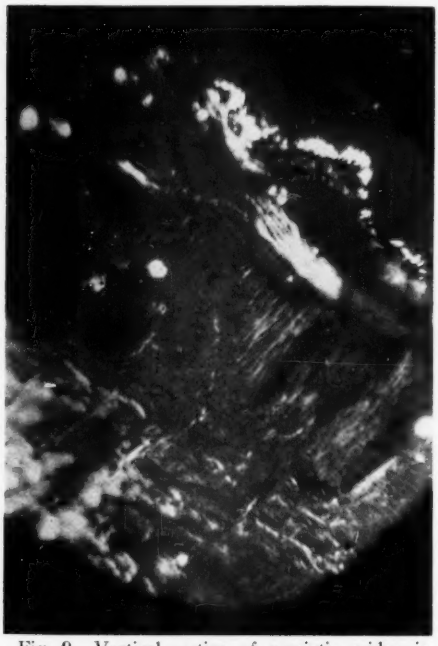


Fig. 9.—Vertical section of psoriatic epidermis, showing persistance of birefringent tonofibrillar system throughout and only a few groups of fibers parallel to the surface, representing the corneal layer; × 200.

intense birefringence of a keratogenous zone is absent. However, in some areas there are fibers running parallel to the surface, though these do not form a coherent layer (Fig. 9).

B. Histochemistry.—In the psoriatic lesion, a Gram-positive zone is seen in the upper third of the epidermis. This zone is increased in width following incubation of the specimen with testicular hyaluronidase.

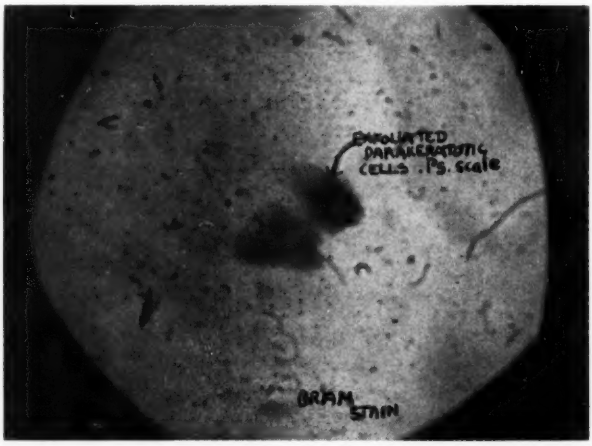


Fig. 10.—Exfoliated parakeratotic cells of psoriatic scale showing variable Gram-positive staining of the cytoplasm; × 1,000.

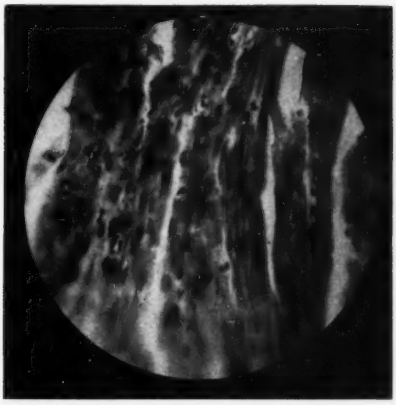


Fig. 11.—Vertical section of psoriatic scale, stained with thionine, showing distribution of metachromatic material within the parakeratotic cells; (*a*) × 200; (*b*) × 900.

The parakeratotic cells of psoriatic scale take up the Gram stain to a variable extent. These cells are never filled with Gram-positive material, there remains a Gram-negative zone at the periphery of their cytoplasm. However, the Gram-positive area is not limited to the cell nucleus and, in some cells where a nucleus cannot be defined, there is still a Gram-positive area (Fig. 10).

In the normal and hyperkeratotic epidermis, the keratohyalin granules are Gram positive and there is some Gram-positive material around the base of the hair follicles. Callus and scales from ichthyosiform erythrodermia are Gram negative.

The fibrous protein isolated from psoriatic scales is Gram negative, while the glycoprotein is Gram positive.

Thionine staining of the psoriatic epidermis reveals a zone of intense metachromasia similar in distribution to the Gram positive area. Many cells in the psoriatic scale contain large amounts of metachromatic material in their cytoplasm, though the degree of metachromasia varies from cell to cell. This metachromasia is destroyed by testicular hyaluronidase (Fig. 11). No metachromatic material is seen in sections of callus or scales from ichthyosiform erythroderma. A few metachromatic granules are seen in the normal epidermis, probably corresponding to keratohyalin granules.

The Alcian blue stain is taken up to a moderate extent by the psoriatic scales, but it appears to be mainly intercellular in distribution, though a few positive granules are seen within the parakeratotic cells.

It does not parallel the distribution of thionine metachromasia. Some Alcian blue-positive material can be seen in scale from ichthyosiform erythrodermia but not in callus. Testicular hyaluronidase does not appear to alter the affinity of psoriatic or other scales for this dye.

Sulfhydryl groups can be demonstrated in psoriatic scale by the Barnnett-Seligman technique. The characteristic staining is intense in this scale, but it is diffuse, and it has not been found possible to localize it

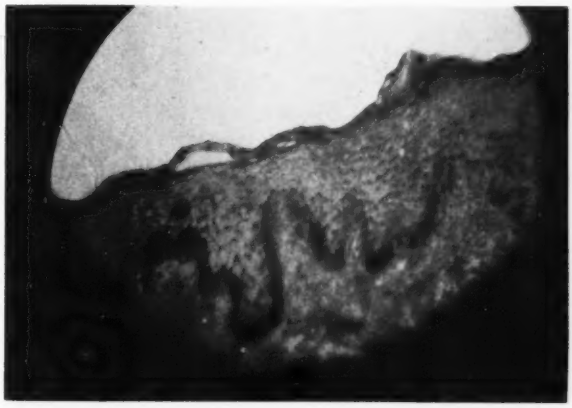


Fig. 12.—Vertical section of psoriatic epidermis showing distribution of sulfhydryl groups; × 400.

within the parakeratotic cells. In the psoriatic epidermis, intense staining occurs in the upper part of the Malpighian layer, as well as in the parakeratotic horny layer (Fig. 12).

Comment

It appears that, in psoriasis, the doubly refractile system of tonofibrils persists throughout the epidermis and is also found in the exfoliated scale, with little modification except for the lateral aggregation of fibers. This is particularly interesting, in view of the previous finding that a fibrous protein can be extracted from psoriatic scale, which is similar to and probably identical with tonofibrin, believed to be the protein of the tonofibrils. Oriented fibers of these proteins have been examined by polarization optical methods and under similar circumstances, their degree of birefringence is identical. This subject will be discussed more fully elsewhere.

Mercer [18] has followed epidermal keratin formation by electron microscopy, and he has described two distinct types of keratinization in normal tissue: an early fibril, without a precursor, corresponding to the tonofibrils, and a later fibril, with keratohyalin as precursor. He has suggested that polarization optical studies support these findings. The fibrils in the lower part of the epidermis, before the appearance of keratohyalin, are weakly birefringent and at right angles to the surface. When keratohyalin transformation occurs, there is a sudden rise in birefringence and orientation is more nearly parallel to the skin surface.

However, in psoriasis the granular layer is absent and with it the keratohyalin granules. Therefore, it may be postulated that epidermal keratinization can proceed only from one source, the tonofibrils and thus it remains in an immature condition. The absence of keratohyalin granules in psoriasis is based on histological studies with a light microscope and until we have electron microscopic data, it will be impossible to confirm this theory.

The histochemical findings support previous biochemical work in which mucopolysaccharides and glycoprotein were found in psoriatic scale extracts. Of particular interest is the interpretation of the Gram stain. Fischer [19] has stated, both with relation to micro-organisms and to keratins that the Gram-staining mechanism involves sulfhydryl groups. Libenson and McIlroy [21] were unable to confirm Fischer's claim and were able to show that basic proteins are also not involved. Johnson et al.,[12] in following the Gram staining of cat tongue keratins, showed that toluidine blue staining coincides with Gram-positive areas. They also showed that certain reactive groups of protein are concerned in the reaction, since positive staining is destroyed by deamination. Henry and Stacey have implicated magnesium ribonucleate as the causative agent. However, their findings were not reproduced by MacLeod et al., who,[21] therefore, were of the opinion that magnesium ribonucleate plays a minor part in the Gram reaction.[23] Further, it was shown by Panijel that protein of Ascaris male gametes alone may give a Gram-positive reaction.[24] Johnson and co-workers also showed that in the case of cat-tongue keratins, nucleic acid extraction did not abolish the stain. Our work demonstrated that Gram staining corresponds more or less accurately to the distribution of metachromasia, produced by thionine. This metachromasia is believed to be due to the presence of intracellular glycoprotein and mucopolysaccharides containing ester sulfates. It may be noted that Gram-positivity of the nuclei of the parakeratotic cells is associated with metachromasia.

The Alcian blue staining, demonstrating substances of acidic nature, notably acid mucopolysaccharides, is not similar to the Gram-positive or metachromatic areas in the psoriatic scale and, in this material, Gram staining cannot be related to the presence of sulfhydryl groups directly. The finding that the fibrous protein from psoriasis scale is Gram negative suggests that the Gram stain is not specific for keratins or prekeratins as such; rather, we have ac-

cumulated evidence that in these keratinizing cells, the Gram stain is taken up by the soluble protein, which is involved in the process of differentiation. In these psoriatic cells, it is known that there is a glycoprotein which is Gram positive and the hypothesis is put forward that this material takes the Gram stain.

The role played by this glycoprotein has not been fully established. Sylven [25] has pointed out that ester sulfates seem to play a part in the supply of sulfurous constituents for keratin synthesis and should be regarded as labile sulfur-bearing compounds. Montagna and Hill [26] found that the uptake of labeled sulfate in the rat hair papilla coincided with metachromasia. It was also recently found that sheep can synthesize cystine from sulfate in the hair follicle.[27] Lewis [28] has found that, in the rumen of sheep, sulfate is reduced to sulfide by sulfate-reducing bacteria, and he has suggested that the reduced sulfur is used in the production of sulfur containing amino acids. We may surmise that in normal keratinizing epidermis, mucopolysaccharides containing ester sulphur are hydrolyzed, the sulfates reduced to sulfide and the sulfur built into the keratin molecule. It has been shown that in frozen sections of the normal epidermis Schiff-positive material is present in the stratum lucidum and between the fibrils in the cells of the Malpighian layer, especially in the keratogenous zone.[29]

Further, Braun-Falco et al. have demonstrated intercellular acid mucopolysaccharide, by the Hale-(periodic acid-Schiff), PAS-staining reaction, in the normal Malpighian layer, as well as in certain pathological states.[30]

We do not know the source of these mucopolysaccharides. However, Curran [31] has recently shown that they are elaborated in and around the endothelia of capillaries. In the skin, therefore, they may be formed in connection with the capillaries of the dermis. The capillary dilatation in the upper part of the psoriatic dermis is well known. Braun-Falco has drawn our attention to it again and has noted changes in the dermal ground substance with release of acid mucopolysaccharides.[32] This, he considered, was a process of unmixing or depolymerization with disturbances in the normal combination between proteins and acid mucopolysaccharides.

The ingestion of anticoagulant drugs, such as heparin and dextran sulfate, has been followed on numerous occasions by alopecia and nail changes.[33-35] Tudhope et al.[36] have suggested that these drugs produce their effect by interfering with the normal metabolism of naturally occurring sulfated mucopolysaccharides. Flesch,[37] in reviewing the whole subject of mucopolysaccharides in the human epidermis, has postulated that, not only hair loss from anticoagulant substances, but also hair loss from excessive intake of vitamin A, and the condition called alopecia mucinosa may be due to disturbances of a hypothetical mucopolysaccharide metabolic chain.

The presence of glycoprotein and sulfated mucopolysaccharide in the psoriatic epidermis may represent an abnormal metabolic pattern whereby labile sulfur is not available for incorporation into the keratin molecule.

Perhaps, indeed we have an alternative pathway in which ester sulfate is built up into the glycoprotein and keratin maturation stops at a prekeratin stage, with a sulfur free fibrous molecule. We may speculate from Mercer's observations [18] that this metabolic error prevents the formation and deposition of keratohyalin, though proof of this theory must await experimental evidence.

The psoriatic process remains an enigma. Our findings suggest that it may be valuable to reopen investigations of sulfur metabolism in this disease, directing our attention to sulfatases and their activators, which must be involved in the synthesis of the keratin molecule. Finally, the biochemical relationship of psoriasis to psoriatic arthritis requires elucidation before we can hope to obtain a clear picture of the pathogenesis of this disease complex.

Summary

Polarization optical methods were used to investigate the anomaly in keratin formation existing in psoriasis. It was found that the birefringent tonofibrillar system persists throughout the psoriatic epidermis and in the psoriatic scale.

Histochemical studies were undertaken to localize mucopolysaccharides, glycoprotein, and sulfhydryl groups in psoriatic epidermis and in control material. In particular, a modification of the Gram-Weigert stain was applied, and it was shown that Gram-positivity in the psoriatic scale and epidermis approximately parallels the distribution of metachromasia induced by thionine. It was concluded that there is an accumulation of an abnormal glycoprotein in the psoriatic epidermis.

The relationship of this glycoprotein to the keratinization anomaly was discussed. It was suggested that psoriasis represents a systemic error of sulfur metabolism in which sulfate is built up into the glycoprotein and becomes unavailable for synthesis of sulfur-containing amino acids and, hence, of keratin itself.

1101 N. Broom St.

Addendum

Recent experiments have shown that the substances stained by the Gram method and by thionine are not identical.

REFERENCES

1. Audry, M. C.: Critique anatomique de quelques keratonoses, Ann. dermat. et syph. 4:384-402, 1893.

2. Flesch, P.: Chemical Data on Human Epidermal Keratinization and Differentiation, J. Invest. Dermat. 31:63-73, 1958.

3. Roe, D. A.: The Application of Paper Electrophoresis to the Diagnosis of Psoriasis, Ann. New York Acad. Sc. 73:977-988, 1958.

4. Selby, C. C.: An Electron Microscope Study of Thin Sections of Human Skin: II. Superficial Cell Layers of Footpad Epidermis, J. Invest. Dermat. 29:131-149, 1957.

5. Buckup, H., and Szakall, A.: Über typische Veranderungen des Gehaltes von Horn-schichtextrakten an Lipoiden und Pentosen bei verschiedenen Gewerbedermatosen. Gewerbedermatosen 5: 181-191, 1957.

6. Roe, D. A.: Untersuchungen der epidermalen Glykoproteine und Mukopolysaccharide bei Psoriasis, Derm. Woch. 139(13):321-324, 1959.

7. Paschoud, J. M.; Keller, W., and Schmidli, B.: Untersuchungen über Peptidasen in der gesunden und befallenen von Psoriasiskranken, Arch. klin. u. exper. Dermat. 203:203-216, 1956.

8. Flesch, P., and Esoda Jackson, E. C.: Chemical Changes in Psoriatic Scales, Ann. New York Acad. Sc. 73:989-999, 1958.

9. Flesch, P., and Esoda Jackson, E. C.: Pentoses in Horny Layers: A Simple Color Test for the Diagnosis of Psoriasis, Lecture given at the 19th Annual Meeting of the Society for Investigative Dermatology, June 22, 1958, J. Invest. Dermat. 32:437-444, 1959.

10. Schmitt, F. O.: Tissue Ultrastructure Analysis: Polarized Light Method, in Medical Physics, edited by O. Glasser, Chicago, The Year Book Publishers, Inc., 1947, pp. 1588-1589.

11. Matoltsy, A. C., and Odland, G. F.: Investigation of the Structure of the Cornified Epithelium of the Human Skin, J. Biophys. & Biochem. Cytol. 1:191-196, 1955.

12. Johnson, P. L.; Hoffman, H., and Rolle, G. K.: The Gram Staining Mechanism of Cat Tongue Keratin, J. Histochem. 5:84-90, 1957.

13. Lillie, R. D.: Histopathologic Technic and Practical Histochemistry, New York, The Blakiston Company (division of McGraw-Hill Book Company, Inc.), 1953, p. 286.

14. Goltz, R. W.; Fusaro, R. M., and Jarvis, J.: The Demonstration of Acid Substances in Normal Skin by Alcian Blue, J. Invest. Dermat. 31:183-190, 1958.

15. Barnnett, R. J., and Seligman, A. M.: Histochemical Demonstration of Sulfhydryl and Disulfide Groups of Protein, J. Nat. Cancer Inst. 14: 769-803, 1954.

16. Nieuwmeijer, A. H.: Tonofibrils in Bullous Dermatoses: A Histo- and Cytopathologic Study, Dermatologica 106:279-387, 1953.

17. Matoltsy, A. G., and Sinesi, S. J.: A Study of the Mechanism of Keratinization of Human Epidermal Cells, Anat. Rec. 128:55-63, 1957.

18. Mercer, E. H.: The Electron Microscopy of Keratinized Tissues, in The Biology of Hair Growth, edited by W. Montagna and R. A. Ellis, New York, Academic Press, Inc., 1958, pp. 107-109.

19. Fischer, R., and Larose, P.: Contribution on the Behavior and Structure of the Cytoplasmic Membrane of Bacteria, Canad. J. M. Sc. 30:86-105, 1952.

20. Fischer, R.: The Selectivity of the Gram Stain for Keratins, Experientia 9:20-21, 1953.

21. Libenson, L., and McIlroy, A. P.: On the Mechanism of the Gram Stain, J. Infect. Dis. 97: 22-26, 1955.

22. Henry, H., and Stacey, M.: Histochemistry of Gram Staining Reaction for Micro-Organisms, Proc. Roy Soc., London, ser. B. 133:391-406, 1946.

23. MacLeod, C. M., and Roe, A. S.: Effect of Silicate on Gram Staining and Viability of Pneumococci and Other Bacteria, J. Exper. Med. 103: 453-463, 1956.

24. Panijel, J.: Recherches sur la nature et la signification de la proteine Gram du gamete male d'Ascaris megalocephala, Biochim. et biophys. acta 6:79-93, 1950.

25. Sylven, B.: The Qualitative Distribution of Metachromatic Polysaccharide Material During Hair Growth, Experimental Cell Research 1:582-589, 1950.

26. Montagna, W., and Hill, C. R.: The Localization of S^{35} in the Skin of the Rat, Anat. Rec. 127:163-172, 1957.

27. Hale, W. H., and Garrigus, U. S.: Synthesis of Cystine in Wool from Elemental Sulfur and Sulfate Sulfur, J. Animal Sc. 12:492-496, 1953.

28. Lewis, D.: The Reduction of Sulfate in the Ruman of the Sheep, Biochem. J. 56:399, 1954.

29. Rodriguez-Perez, A. P.: Contribucion al conocimiente histoquimico del epitelio cutaneo, Actas-dermo-sifiligr 47:273-281, 1956.

30. Braun-Falco, O., and Weber, G.; Zur Hist- und Biochemie des epidermalen Intercellularraumes unter normalen und pathologischen Verhaltnissen. Arch. klin. u. exper. Dermat. 207:459-471, 1958.

31. Curran, R.: The Elaboration of Mucopolysaccharides by Vascular Endothelium, J. Path. Bact. 74:347-352, 1957.

32. Braun-Falco, O.: The Histochemistry of Psoriasis, Ann. New York Acad. Sc. 73:936-976, 1958.

33. Engelberg, H.; Kuhn, R., and Steinman, M. A.: Controlled Study of the Effect of Intermittent Heparin Therapy on the Course of Human Coronary Atherosclerosis, Circulation 13:489-498, 1956.

34. Wright, I. S.: An Evaluation of Anticoagulant Therapy, Am. J. Med. 14:720-730, 1953.

35. Hirschboeck, J. S.; Madison, F. W., and Pisciotta, A. V.: Alopecia and Other Toxic Effects of Heparin and Synthetic Heparinoids, Am. J. Med. Sc. 227:279-282, 1954.

36. Tudhope, G. R.; Cohen, H., and Meikle, R. W.: Alopecia Following Treatment with Dextran Sulfate and Other Anticoagulant Drugs, Brit. Med. J. 5078:1034-1037, 1958.

37. Flesch, P.: Mucopolysaccharides in Human Epidermis, J. Soc. Cosmetic Chemists, to be published.

38. Roe, D. A.: Unpublished data.

Clinical Notes, New Instruments and Techniques

Double-Blind Evaluation of Trimeprazine

An Oral Antipruritic

IRVING D. LONDON, M.D., Montgomery, Ala.

Recently, a phenothiazine derivative, trimeprazine (Temaril *), was reported on [1] in fairly glowing terms as being valuable in the relief of itching when taken orally. For example, Callaway and Olansky [1] found that 82% of their patients with various skin conditions obtained good or excellent relief of itching while taking the drug. Because of Kligman's [2] criticism of the lack of controlled, double-blind studies in the enthusiastic reports on trimeprazine, I was stimulated to determine whether the antipruritic effects ascribed this drug would stand the rigors of a controlled, double-blind evaluation.

Patient Selection

This study was carried out in 104 patients (33 males and 72 females) from private practice, who ranged in age from 10 years to 88 years. All the patients were selected on the basis of severe itching associated with common dermatologic, allergic, or systemic disorders. In general, itching had been present for periods varying from a week to several years or more, and many patients had taken other drugs previously with poor results. For purposes of tabulation, the patients were grouped according to the primary cause of their itching as follows: (1) neurogenic pruritus, (2) allergic pruritus, and (3) varied pruritus (pruritus in this group was associated with a variety of common dermatoses).

Method

Trimeprazine was supplied as a 2.5 mg. coated, gray tablet; an identical tablet containing calcium sulfate was supplied as the placebo. Fifty-eight patients received trimeprazine as a first course of therapy; 46 received the placebo. Neither the physician nor the patient knew which tablet was being used during the course of the test.

Patients were instructed to take one tablet after meals and at bedtime and to double or triple the bedtime dose, if necessary. Observations and interviews with the patients to determine the response to treatment were made at intervals of from five to seven days. The efficacy of the medications was determined at the end of therapy, which averaged three weeks. In 24 patients, the medications were alternated without the physician knowing which was being given.

Blood and liver-function studies were not carried out routinely, since trimeprazine was given for relatively short periods of time and in comparatively small doses. Previous studies [3] on hospitalized patients taking up to 40 mg. of trimeprazine daily (four times the dose used in this study) had shown the drug to be free of photosensitivity reactions and of other toxic effects.

Submitted for publication Nov. 18, 1958.

* Chemically, trimeprazine is *dl*-10(3-dimethylamino-2-methylpropyl) phenothiazine.

TABLE 1.—*Results of Controlled, Double-Blind Study Comparing Trimeprazine with a Placebo* *

Indication	No. Treated	Results							
		Placebo				Trimeprazine			
		Exc.	Good	Fair	Poor	Exc.	Good	Fair	Poor
Neurogenic pruritus	68	9	6	3	13	27	5	3	2
Allergic pruritus	11	1	0	0	3	5	1	1	0
Varied pruritus	25	3	2	2	4	6	3	1	4
Totals	104	13	8	5	20	38	9	5	6
		45%		55%		81%		19%	

* $\chi^2 = 14.18 - P = < 0.001$

Results

Results were classified according to the criteria of Callaway and Olansky,[1] as follows: excellent, complete relief of itching; good, substantial relief; fair, some relief; poor, no relief. The results are given in Table 1, together with the results of the standard two-celled χ^2 test that was used to analyze the data statistically. As will be noted, patients receiving trimeprazine obtained significantly better results than those receiving the placebo.

When itching was controlled, the rapidity of action, response to increased doses, and the incidence of side-effects varied so little it was impossible to distinguish which patients had been given the placebo. This seems to indicate that "true" placebo reactors mimic, in every way, the actions ordinarily obtained with an active drug. Other investigators have described this observation. In some patients, particularly those with long-standing dermatoses, the relief of itching was dramatic. Uncontrollable bouts of scratching were rare during therapy, and many of the patients slept better for the first time in several weeks. After the code to the study was revealed and the results for each patient had been reviewed, it was evident that the most outstanding antipruritic effects had been experienced by the patients when they were receiving trimeprazine.

The results of the crossover tests in which 24 patients received the placebo and trimeprazine alternately are grouped in Table 2. Of the 20 patients who received placebo first, 5 obtained adequate relief of itching, whereas 17 of them obtained complete or substantial relief when taking trimeprazine. A statistical test (two-celled χ^2 test) of the data on the first line of this table gives a χ^2 value of 18.54. The corresponding probability value is less than 0.001 and indicates that the results produced by trimeprazine are statistically superior to those produced by the placebo. According to the statisticians who analyzed and checked all the data in this report, there were too few patients who received trimeprazine as a first course of therapy (Line 2 of Table 2) to permit a valid statistical test of these data. I believe now that all the patients should have received both drugs alternately.

TABLE 2.—*Grouping Results of Crossover Study of Patients Receiving Either Placebo or Trimeprazine as a First Course of Therapy*

	No. Treated	Results			
		Exc.	Good	Fair	Poor
First course of therapy					
Placebo	20	3	2	3	12
Trimeprazine	4	0	0	2	2
Second course of therapy					
Trimeprazine	20	12	5	0	3
Placebo	4	1	1	0	2

Side-Effects

Six of the patients reported the side-effects (drowsiness, three; nervousness, two; lethargy, one) while receiving trimeprazine; four patients reported side-effects (urticaria, one; nausea, one; dizziness, one; "grogginess," one) while taking the placebo. The medications were discontinued in all these patients. There was no clinical evidence of photosensitivity, jaundice, or any other serious reaction during the evaluation.

Comment

Relief of itching and, concurrently, the ability to sleep as a result thereof were dramatic in many of the patients after the administration of trimeprazine. It is not, however, a "cure," and the relief of itching alone did not clear up old, long-standing lichenified patches of neurodermatitis or chronic vesicles of dishydrotic eczema. However, once the patient was relieved of his primary complaint, it was comparatively simple to follow up with more definite treatment of the involved areas. The mechanism by which trimeprazine controls itching is unknown. It probably acts on the central nervous system to reduce itch perception.

Mr. Virgil M. McIntosh, Analytical Statistician, Maxwell Air Force Base, and Dr. Eldredge Scales, Director of Institutional Research, Tuskegee Institute, Ala., helped with the statistical analyses included in this report.

122 S. Ripley St. (5).

REFERENCES

1. Callaway, J. L., and Olansky, S.: Trimeprazine: An Adjuvant in the Management of Itching Dermatoses, North Carolina M. J. 18:320-321, 1957.

2. Kligman, A. M.: Paper presented at the meeting of the American Academy of Dermatology, Chicago, Dec., 1957.

3. Cahn, M. M.: Personal communication to the author.

Ingrown Hairs of the Bearded Areas of the Face and Neck

C. RUSSELL ANDERSON, M.D., Beverly Hills, Calif.

For many years I have instructed my patients who suffer from ingrown hairs of the bearded areas of the face and neck to brush briskly the affected areas at night with a stiff-bristled nail brush, brushing against the direction of the growth of the beard. I never manually epilate the ingrown hairs except those in granulomatous nodules. I also forbid the patient to epilate manually the ingrown hairs. This simple routine always solves this troublesome problem.

Submitted for publication Jan. 27, 1959.

416 N. Bedford Dr.

A New Phenolated Scalp Oil

LEON GOLDMAN, M.D., and ROBERT H. PRESTON, M.D., Cincinnati

The value of mineral oils containing phenol for the treatment of various common disorders of the scalp, especially psoriasis, has been shown by Vickers,[1] Sulzberger and Obadia,[2] and recently, in our department, by Goldberg and Barnett.[3] These materials are easier to use than messy greasy ointments. The difficulty has been to obtain a stable, homogeneous suspension of phenol in the mixture and also a cosmetically suitable material. An improvement over the older phenolated oil mixtures has been developed recently by the addition of surfactants to a vehicle of oil derived from lard instead of from mineral oil. This makes for a stable suspension. The mixture is also perfumed. Because of the recent interest in the disturbed protein metabolism of the epidermis in psoriasis, an acylated amino acid has been added to the mixture. The concentration of phenol is approximately 2%. A medication for psoriasis must be strong. The technique of use has been the gentle application with cotton applicators on the scaling areas of the scalp twice daily. Care should be taken to avoid excessive amount on the forehead, neck, or ears to avoid irritation. These areas may be protected by a bland cream. Large amounts should not be used, otherwise the head becomes too greasy. The material has also been put on thick spots of psoriasis on the body, psoriasis of the palms, and around psoriasis of the nails. In this latter condition, the phenolated oil is employed primarily to keep the skin about the nails soft. It can be used also for seborrheic dermatitis of the scalp of the dry type but not for acute seborrheic dermatitis. In senile pruritus of the scalp, this oil may be spotted on sparingly as desired by the uncomfortable patient. This material can be used also as a hair dressing in psoriasis of the scalp. This effective suspension is tolerated well by the scalp. In a series of 142 cases there has been only one case of contact dermatitis in a young child when the oil mixture was applied on psoriasis with secondary neurodermatitis of the ankle. Patch tests revealed a sensitivity to the lard oil. The patient had complained of previous difficulties with contact with certain types of oils. There were three other cases of mild irritant reactions about the forehead and neck. The patch tests in these cases were negative. This appeared to be primary irritation reaction. This phenolated oil is too strong to be used as an antipruritic body oil. Trials were also made of this material as a vehicle for liquor carbonas detergens and sulfur. Phenolated scalp oil can also be colored easily.

Submitted for publication Dec. 11, 1958.

From the Department of Dermatology, University of Cincinnati College of Medicine.

Phenolated oil (Sarcophen) furnished by I. B. Wershaw, Dome Chemicals, Inc., New York.

Department of Dermatology, Cincinnati General Hospital.

REFERENCES

1. Vickers, M. A.: The Clinical Evaluation of a Liquid Suggested for Psoriasiform Problems of the Scalp, J. Maine M. A. 45:332 (Dec.) 1954.

2. Sulzberger, M., and Obadia, J.: A Modified Liquid Petrolatum Preparation, A. M. A. Arch. Dermat. 73:373 (April) 1956.

3. Goldberg, L. L., and Barnett, S. M.: Treatment of Cutaneous Problems with a Carbolated Medication, Antibiotic Med. 4:59 (Oct.) 1957.

Partial Alopecia Due to Thallium

W. R. HUBLER, M.D., Corpus Christi, Texas

During the past two and one-half years, I have observed 13 cases of slight to moderate alopecia from the ingestion of thallium. The first five were in small children who had eaten varying amounts of a cake-crumb roach killer containing thallium.* During this period there were approximately 40 reported cases of thallium poisoning in small children in Corpus Christi from the same preparation. Legal action was taken by the County Medical Society to force the manufacturers of the roach killer to include a bitter-tasting substance to make the cake-crumb preparation less attractive to children. Since this has been done, I have seen only two cases of thallium alopecia in children. I have, however, observed six cases of slight to almost complete diffuse alopecia in women. The diagnosis was proved in all cases by spectroscopic examination of the patient's urine for thallium. If it had not been for the previously mentioned "epidemic" of hair loss, I might never have suspected these women of having hair loss due to thallium. In none of my cases was there any ataxia, tremor, or other toxic manifestation of thallium poisoning.[1] Careful investigation has failed to reveal the source of the thallium in these cases. None of the women used any insect poisons known to contain thallium. The Health Department has suggested several possible sources of thallium in these cases:

(*a*) Ingestion of bread made with flour which might have been accidentally contaminated with a thallium insecticide.

(*b*) Thallium dust (insect powder) present on the tops of cans of food.

(*c*) Contact † with or ingestion of thallium used by professional exterminators. The exterminators are not supposed to use thallium in their pesticides, but this has not been enforced.

All of my adult patients were women. Perhaps this was because the average man does not pay close attention to mild or moderate hair loss, ascribing it to the natural course of events. The duration of "falling hair" before the diagnosis was made varied from one to four months. The cessation of hair loss and the beginning of regrowth usually occurred in four to eight weeks after the first visit. The duration of the symptoms would make me suspect that more than one small dose of thallium was ingested by some of the patients.

The purpose of this note is to call attention to the possibility that unexplained hair loss in adults may be due to thallium ingestion. Perhaps it is commoner than has been realized, particularly in warmer sections of the country where insecticides are used to a greater extent. The diagnosis is easily proved by spectroscopic examination of the urine.

1510 S. Brownlee Blvd.

Submitted for publication Feb. 25, 1959.

* "Echols Roach Killer," available in all the Corpus Christi supermarkets, is made by saturating crushed cookies or cake crumbs with a 2% aqueous solution of thallium, which is tasteless.

† Thallium may be absorbed through the unbroken skin.

REFERENCE

1. Chamberlain, P. H., et al.: Thallium Poisoning, Pediatrics *22*:1170-1182, 1958.

A New Shampoo for Seborrheic Dermatitis

LEONARD V. KORNBLEE, M.D., New York; ARTHUR H. GLADSTEIN, M.D., Astoria, N. Y., and PAUL LAZAR, M.D., Chicago

Experience with N-trichloromethylmercapto-4-cychlohexane-1,2-dicarboximide has proved it to be an effective and safe remedy for seborrheic dermatitis.[1] Keeping the chemical in permanent solution has been a technical problem which may have decreased its effectiveness. For the first time, the chemical in stable solution has been incorporated in a detergent shampoo * which contained also, sodium tetrathionate, a source of sulfur, and *p*-chloro-xylenol,[2,3] an antibacterial agent. Each of these chemicals has been used and tested ex-

Submitted for publication Jan. 26, 1959.

* The shampoo, Clear Liquid Enden, was supplied by Helene Curtis Industries, Inc.

Results of Treatment with Shampoo

Response	Study A { M 20 F 30	Study B { M 15 F 22	Study C { M 40 F 83	Total { M 75 F 135
	Subjects/%			
Poor	2/4	1/2.7	1/0.8	4/1.9
Moderate	6/12	8/21.5	31/25.2	45/21.4
Good	41/82	12/32.3	44/35.8	97/46.2
Excellent	1/2	16/43.5	47/38.2	64/30.5
Total	50/100	37/100	123/100	210/100

tensively and demonstrated to be nontoxic, as well as low in sensitizing potential.

A total of 210 patients from private practice (135 females and 75 males), ranging in age from 8 months to 73 years, used the shampoo for a period of eight weeks each. Every person was examined on at least three or four occasions during this period and again two weeks or more after use of the shampoo was discontinued.

Good to excellent results were noted from its use in 161 (76.5%) of those treated; 45 (21.4%) had improvement which was not sustained despite continued therapy, and 4 (1.9%) were considered failures. The unsatisfactory results occurred in persons with very thick, adherent scales (psoriasis?), a situation not generally well handled by dandruff treatment shampoos. When recurrence was evident, signs and symptoms were noted 10 to 14 days after the shampoo was discontinued.

No primary irritation, allergic reactions, or chemical incompatibilities were observed. Excessive oiliness was seen in three instances. This disappeared after one week, though the patients continued to use the shampoo.

The study was conducted independently in the private practices of three different physicians in widely separated areas. Control studies on 37 persons showed the combined formulation to be superior to the detergent shampoo alone. The preparation is as effective as any of the available dandruff treatment shampoos, more pleasant cosmetically than most and is a worthwhile adjunct remedy for the treatment of seborrheic dermatitis.

104 S. Michigan Ave., Chicago (3).

REFERENCES

1. Ball, F. I.: A New Treatment for Seborrheic Dermatitis, A. M. A. Arch. Dermat. & Syph. 71:696-698, 1951.

2. Zondek, B., and Finkelstein, M.: Blood Concentration of *p*-Chloro-Xylenol in Man Following Percutaneous, Parenteral and Rectal Application, Proc. Soc. Exper. Biol. & Med. 61:200-203, 1946.

3. Colebrook, L.: The Disinfection of the Skin, Bull. War Med. 2:73-79, 1941.

Azure Lunulae

IRVING L. LEFF, M.D., Buffalo

Bluish discoloration of the nails has been reported in different conditions and under a variety of circumstances. The whole nail is discolored in argyria[1,2] after prolonged use of quinacrine hydrochloride,[3] in paronychia caused by Pseudomonas aeruginosa,[4,5] and on exposure to sunlight following soaking in bichloride of mercury.[6] Discoloration in argyria occurs in association with involvement of skin and mucous membranes and does not disappear with the passage of time in contrast to the latter three circumstances where removal of the cause is followed by gradual disappearance of the discoloration.

Bluish coloration limited to the lunule of the nail was noted by Campbell, in 1931, following use of phenolphthalein.[7] The fate of the discoloration in this case with the passage of time is not mentioned. More recently, Bearn and McKusick observed the phenomenon in two cases of Wilson's disease[8] and reported a third case seen by Dr. I. Herbert Scheinberg.

These latter cases exhibited classic clinical and/or chemical evidence of Wilson's disease with low serum copper and ceruloplasmin, elevated urinary copper and amino acids, and increased urinary cop-

Submitted for publication Jan 22, 1959.

From the Medical Service of the Buffalo Veterans Administration Hospital.

per excretion on administration of penicillamine. The copper content of the fingernails with azure lunulae did not differ significantly from control cases of Wilson's disease and ordinary cirrhosis. Although the blue discoloration was thought possibly related to increased body copper, the pathogenesis and localization of the discoloration could not be elucidated.

We wish to report another case of azure lunulae which could not be related to any of the previously observed conditions.

Report of a Case

A 65-year-old white retired grain weigher was admitted in July, 1956, to the Medical Service of the Buffalo Veterans Administration Hospital with a four-month history of effort dyspnea, easy fatigability, and occasional cough productive of scant brownish sputum, accentuated in the few days prior to admission by fever, chilly sensations, and prostration.

He had retired a year previously after 36 years as a grain weigher, during which time it is believed he used powdered calcium cyanide as a fumigant and liquid grain fumigants, such as ethylene dibromide. His parents are dead, but he recalls nothing unusual about their fingernails. His three children and a sibling are likewise unaffected.

Azure lunulae of the fingernails.

On admission, azure lunulae of the fingernails were noted (Figure) which the patient claimed had been present as long as he could remember. The color did not fade on application of pressure to the nail bed. Examination of the lungs revealed atelectasis and pneumonia of the right middle lobe. Bronchoscopy revealed narrowing of the right middle lobe bronchus and compression of the lung root was suspected. However, clearing occurred slowly on parenteral antibiotics and bronchodilator aerosols. Good health has been maintained during a two-year follow-up, and the appearance of the nails is unchanged. A serum copper determination, performed during a recent visit, was normal and liver-function tests unremarkable.

Comment

The azure lunulae in this case appear to be an individual variant of no clinical significance. The national grain company which employed him has encountered no instances of this phenomenon in other workers similarly employed in elevators and indicates that exposure to the chemicals used is in trace amounts and for very limited periods of time, usually measured in minutes.[9] Symptoms of acute and chronic poisoning to these agents have been well documented.[10] They do not include anything resembling azure lunulae. As for the reported association with Wilson's disease, another investigator of this disease[11] has not noted any fingernail discoloration in numerous patients with hepatolenticular degeneration he has seen.

Blue discoloration of the skin is produced by "scattering" of light by pigment of whatever nature.[12] This is true both of foreign pigment and of normal endogenous pigment, such as that of the eye which is responsible for the blue sclerae of ossium fragilitas by virtue of the abnormal transparency of the sclera to light in this condition. The appearance of normal "blue" veins beneath the skin is another example of the modification of the hemoglobin containing vessels, when observed under transmitted and scattered light but which are red under direct vision. It is conceivable that a combination of just the right degree of transparency of the nail with a fortuitous arrangement of the blood vessels at the base of the nail might result in the phenomenon of azure lunulae without the presence, necessarily, of any disease process, though the failure to fade on pressure militates against this explanation.

Summary

A case of azure lunulae of the fingernails is presented, occurring in an apparently normal person and presumably unrelated to any of the states previously associated with the condition.

Veterans Administration Hospital, 3495 Bailey Ave.

REFERENCES

1. Wright, I. S.: Clinical Value of Human Capillary Studies in Fever, Mental Deficiency, Nephritis, Vascular Diseases, Clubbed Fingers, Arthritis, Tobacco Smoking and Argyria, J. A. M. A. 101:439-442 (Aug. 5) 1933.

2. Harker, J. M., and Hunter, D.: Occupational Argyria, Brit. J. Dermat. 47:441-455 (Nov.) 1935.

3. Lutterloh, C. H., and Shallenberger, P. L.: Unusual Pigmentation Developing After Prolonged Suppressive Therapy with Quinacrine Hydrochloride, Arch. Dermat. & Syph. 53:349-354 (April) 1946.

4. Bauer, M. F., and Cohen, H.: Role of Pseudomonas Aeruginosa in Infections About the Nails, A. M. A. Arch. Dermat. 75:394-396 (March) 1957.

5. Moore, M., and Marcus, M. D.: Green Nails: Role of Candida (Syringospora, Monilia) and Pseudomonas Aeruginosa, A. M. A. Arch. Dermat. 64:499-505 (Oct.) 1951.

6. Callaway, J. L.: Transient Discoloration of Nails Due to Mercury Bichloride, Arch. Dermat. & Syph. 36:62-64 (July) 1937.

7. Campbell, G. G.: Peculiar Pigmentation Following Use of Purgative Containing Phenolphthalein, Brit. J. Dermat. 43:186-187 (April) 1931.

8. Bearn, A. G., and McKusick, V. A.: Azure Lunulae, J. A. M. A. 166:904-906 (Feb. 22) 1958.

9. Wagner, G. B.: Personal communication to the author.

10. Fairhall, L. T.: Industrial Toxicology, Ed. 2, Baltimore, Williams & Wilkins Company, 1957.

11. Homburger, F.: Personal communication to the author.

12. Jeghers, H., and Edwards, E. A., in Signs and Symptoms, edited by C. M. MacBryde, Ed. 2, Philadelphia, J. B. Lippincott Company, 1952, p. 704.

A Technique for Intravenous Therapy in Patients with Scleroderma and in Apprehensive Children

JOHN S. LUNDY, M.D., Rochester, Minn.

Every physician has seen, at times, a patient's morbid dread of a relatively minor therapeutic procedure which normally is accompanied by no risk whatever. Sometimes, confronted with the need for repeated venipuncture, an apprehensive patient may even ask to be dismissed and sent home without any treatment. On the other hand, it is common, in such an instance, to witness the great relief and disappearance of anxiety in the patient once the procedure has been carried out or, even more strikingly, once it is decided that repetition of the much-feared procedure is not necessary.

Such is certainly true of venipuncture in the minds of many patients. When a person who has scleroderma requires intravenous therapy, the trepidation and anxiety are compounded over and over again as the patient is faced with the knowledge that the needle may have to be reintroduced a number of times. The technique which I shall describe concerns a means for the institution of intravenous therapy which has reduced fear and disquiet among such patients and also among small children whose prime reaction to what they do not understand is fright or foreboding.

Part of the present-day treatment of scleroderma is the intravenous administration of edathamil disodium (Endrate). A number of treatments are required over a period of days, and sometimes venipuncture is difficult. Often I have been asked by my colleagues to help emplace the needle.

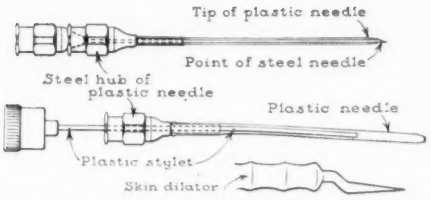
Recently, I developed the following procedure to ameliorate this undesirable situation. An intradermal wheal is raised with a local anesthetic agent. This action of course is more painful among patients with scleroderma than among patients with normal skin, but it is important to make the wheal. I then make a hole through the skin with a dilating instrument. My instrument of choice is a skin dilator that I have devised.* It is true that a large needle (13 gauge) could be used for this purpose, but the needle will cause more bleeding than the dilator causes.

The hole through the skin is made somewhat to one side of the vein in question so that the vein is not injured by the action. In this way I have eliminated the problem scleroderma presents so far as venipuncture is concerned, because the needle

Submitted for publication Jan. 13, 1959.

Section of Anesthesiology, Mayo Clinic and Mayo Foundation. The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota.

* This dilator can be obtained from V. Mueller & Company, Rochester, Minn.



The plastic needle and plastic stylet employed in the technique described, with a representation of the skin dilator.

can be inserted through the hole in the skin, moved against the wall of the vein, and then inserted into the lumen of the vein. Consequently, now that the plastic stylet for the plastic needle is available[1] (Figure), it is a very simple matter to leave the plastic-styleted needle in situ in the vein until the treatments have been completed. The need for repeated introduction of the needle is thus abolished.

If thrombophlebitis should chance to develop, the plastic needle should be removed and a different vein should be used.

The method represents a considerable convenience to all concerned. It allows the patient, between treatments, to take care of herself or himself. It permits the patient to get out of bed, to go to the bathroom, to take physical therapy, and, in general, be free from the bottle and dripper and fluids which otherwise, during intravenous therapy, must run continually to keep the ordinary needle open.

The indwelling needle had to be removed from one patient whose arm became sore, hot, and swollen. In this instance the vein was tender after three and one-half days. The longest time that I have been able to keep a plastic-styleted needle in a vein was 30 days. The patient was a 10-year-old child who had leukemia. Repeated venipuncture, of course, had become a problem, yet the needle remained in place for 30 days with no sign of inflammation. Such tolerance is unusual. The only explanation of it may be that the child was being treated with cortisone. If such indeed is the true explanation of such uncommon tolerance of an indwelling needle, possibly all patients who must receive prolonged intravenous therapy should receive some cortisone with an antibiotic agent; the combination might increase the tolerance of the patient to the needle.

It is surprising how much relief is exhibited by the parents of children when this method is used, especially when the children are crying because of fright at the taking of samples of blood by the pediatrician or some other practitioner. Parents and relatives in such instances are effusive in their gratitude to the physician in charge.

Mayo Clinic.

REFERENCE

1. Lundy, J. S.: Plastic Stylet for Plastic Needle, Proc. Staff Meet. Mayo Clin. 33:458-459 (Sept. 17) 1958.

Removal of Linear Scars

JOHN J. McANDREW, M.D., Orlando, Fla.

Dermabrasion has become a function of the dermatologist, as well as the plastic surgeon. Linear scar removal, however, is generally considered to be the prerogative of the plastic surgeon.

A method of removal of linear scars is presented. With this method many linear scars can be removed simply as an office procedure. Moreover, the results of their removal will compare favorably with those of more elaborate methods.

This method is not new. It is in wide current usage by plastic surgeons. The surgical principle involved has been touched upon in our literature only by Strauss and Kligman[1] in a reference to the work of Iverson.[2] To my knowledge, it is not mentioned in our texts, surgical or otherwise, and it is not sufficiently known about among dermatologists.

Submitted for publication Jan. 19, 1959.

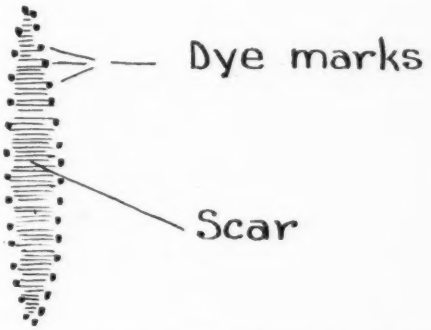


Fig. 1.—Linear scar outlined with dye into the dermis.

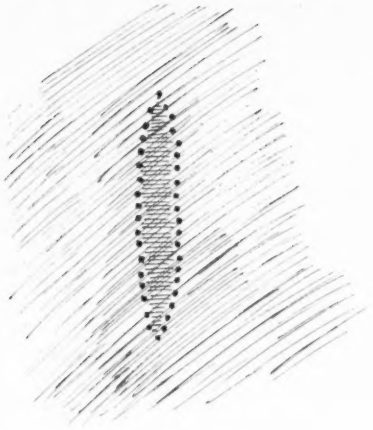


Fig. 2.—Epidermis removed from scar and surrounding area by dermabrasion. Dermal portion of scar remains outlined with dye marks.

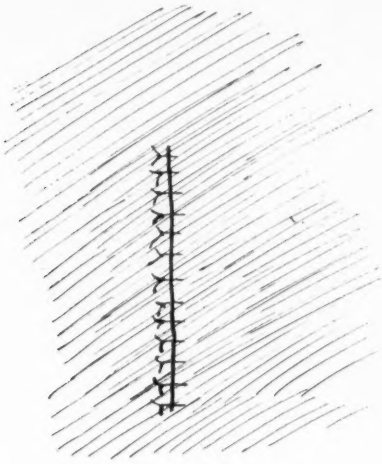


Fig. 3.—Scar (including dye marks) excised. Sutures placed. Future epidermis will cover the sutures, thereby avoiding usual suture marks.

This method is only a slight modification of the one suggested by Iverson.[3] It consists of the following steps:

1. Infiltrate the area with a solution of procaine (1%) and epinephrine (1:200,000).

2. Outline the scar by making perforations with a needle dipped in methylene blue. This serves as an accurate guide for excision after the epidermis of the scar and surrounding skin has been removed.

3. Dermabrade the surface of the linear scar and the surrounding skin beyond the limits of any sutures to be placed after the removal of the scar.

4. Remove the scar as outlined by the dye and suture the dermis defect together carefully with a fine smooth suture material. Iverson[3] likes Dermalon 5-0.

5. Leave the sutures in for about 10 to 14 days. In this time the epidermis has regenerated about the sutures as well as over the abraded area. The crust over the abraded area should not be disturbed. The sutures should be carefully teased out and cut with ophthalmic scissors so as to disrupt the epidermis as little as possible.

6. Dressings may be of Telfa immediately postoperatively. These dressings may be removed after the first 24 hours.[4] An alternative recommendation in postoperative dressing is to utilize a grease-gauze dressing (Aureomycin [chlortetracycline] ointment), which is not removed for six to nine days.

7. Protect the operative area from physical and chemical trauma as long as the postoperative erythema persists.

21 W. Columbia.

REFERENCES

1. Strauss, J. S., and Kligman, A. M.: Acne, A. M. A. Arch. Dermat. 74:397-404 (Oct.) 1956.

2. Iverson, P. C.: Further Developments in the Treatment of Skin Lesions by Surgical Abrasion, Plast. & Reconstruct. Surg. 12:27-40 (July) 1957.

3. Iverson, P. C.: Dermal Abrasion, Am. J. Nurs. 57:860-864 (July) 1957.

4. Burks, J. W., Jr.: Personal communication to the author.

Onset of Psoriasis During the Course of Steroid Therapy

SAMUEL J. ZAKON, M.D., and FRED LEVIT, M.D., Chicago

In a recent publication Shelley and Harun[1] reported that triamcinolone (9-α-fluoro-16-α-hydroxyprednisolone) has been shown to have a significant temporary supressive effect on psoriasis. While Baer and Witten do not advocate the use of steroids as a routine treatment of psoriasis they did express the hope: ". . .with the development of newer analogues of cortisone it is entirely possible that this situation may change. For example triamcinolone appears to be more effective (in equivalent doses) in the management of psoriasis than the other corticosteroid drugs. Doses as small as 8 to 16 mg. daily may produce striking improvement in psoriasis vulgaris. . . ."[2]

We have a patient under observation who developed his first lesions of psoriasis while taking prednisone and triamcinolone for intractable asthma. Hence, it would indicate that these steroids could not even suppress the onset of psoriasis. To our knowledge no similar case has previously been reported.

Report of a Case *

A 55-year-old white male ventilation engineer was well until 1944, when he was hospitalized for a bronchial infection. In 1946, he had a recurrence of symptoms and a diagnosis of asthma was made. He was given many different medications and, in 1950, was again hospitalized. At this time he was treated with cortisone for several days.

He did not again receive steroid therapy until 1952, when he was once again treated with cortisone. Since then he has been continuously taking corticotropin (ACTH) or one of the steroids. He has been on cortisone, hydrocortisone, and, more recently, on prednisone and triamcinolone. The dosages have varied from 1 to 6 tablets a day.

Except for a pustular eruption which appeared on his face when he was given potassium iodide for his asthma, he had no other skin lesions throughout his life. There is no family history of psoriasis. In October, 1958, he first noted scaly patches on the scalp and leg. At that time he was taking prednisone in doses of 8 to 24 mg. daily. Shortly after the onset of his skin lesions, his steroids were changed to triamcinolone, and he has been taking 4 to 16 mg. daily. He did not notice any improvement in his skin eruption when the dosage of the drug was increased to 16 mg. daily. New lesions were appearing, and the older ones gradually grew larger.

When first seen by us, on Jan. 17, 1959, he presented patches of psoriasis on the scalp, elbows, extensor aspect of the left leg, chest, and back. They were dry erythematous plaques covered with a silvery scale. Auspitz sign was readily elicited from one of the lesions. There was some improvement of the lesions after several days treatment with 5% ammoniated mercury ointment.

Comment

We agree with Shelley et al.:

"Triamcinolone in common with all other antipsoriasis remedies is no cure for psoriasis. It must be recognized as purely palliative. Its use must reflect this fact. . .triamcinolone is a strong corticosteroid with influence throughout the entire body. It is not to be given for the relief of a few scales on the elbows."

This patient has been taking steroids for six years. During that time he has frequently been taking moderately high doses. That this failed to prevent the onset of psoriasis at this time is of course apparent. It is a matter of speculation whether or not the disease might have erupted sooner had he not been taking steroids.

Summary

A 55-year-old man developed lesions of psoriasis for the first time while taking steroids for asthma. The eruption appeared after six years of continuous steroid therapy while he was taking prednisone and progressed while he was taking triamcinolone.

Department of Dermatology, Northwestern University Medical Center.

REFERENCES

1. Shelley, W. B.; Harun, J. S., and Pillsbury, D. M.: The Treatment of Psoriasis and Other Dermatoses with Triamcinolone (Aristocort), J. A. M. A. 167:959, 1958.

2. Baer, R. L., and Witten, V. H., Editors: The Year Book of Dermatology and Syphilology, Series 1957-1958, Chicago, The Year Book Publishers, Inc., 1958, p. 47.

Submitted for publication Feb. 5, 1959.

Department of Dermatology, Northwestern University Medical Center (Herbert Rattner, M.D., Chairman).

* This patient was presented at the Jan. 21, 1959, meeting of the Chicago Dermatological Society.

Nail Changes Due to New Base Coat

MILTON REISCH, M.D., New York

Cosmetic companies have been trying for many years to produce a base coat for nail polish which will make the lacquer more durable. Solutions of synthetic rubber, aryl sulfonamide formaldehyde resin, and phenol formaldehyde resins in methyl ethyl ketone have been used as an undercoat on the nail before the application of nail polish or lacquer. Subungual and ungual changes have occurred consisting of discoloration of the nail plate, separation of the distal edge from the bed, hyperkeratotic material under the free edge, erythema, edema, and scaling of the skin of the finger tips. Paronychia has also been reported. Patch tests to the resin and rubber solutions were positive, and the dermatitis was felt to be a distinctive form of eczematous contact dermatitis involving the nail bed.[1,2]

Recently a new undercoat * has been introduced. Nail changes due to it have been noted consisting of discoloration, separation of the nail plate, and tenderness of the finger tips. These changes are possibly due to the occlusive nature of the undercoat rather than an eczematous contact dermatitis. The manufacturer states that the 22 ingredients making up the undercoat do not contain any synthetic rubber or formaldehyde resins.

Following is a report of a case demonstrating an instance of nail changes due to a new undercoat.

Report of Case

A 48-year-old white woman had her fingernails manicured and polished without the use of a base coat for many years. About four months ago, she had a manicure. After the previous nail polish was removed, cuticle remover was applied and removed. The new base coat * was applied, followed by nail polish. Two weeks later the same procedure was repeated. Two weeks later, while removing the nail polish the manicurist noted discoloration of the right thumbnail. She asked the patient about a possible injury. The base coat was again applied, followed by the polish. Two weeks later, on removal of the nail polish, changes

Fig. 1.—Thumbnails.

Submitted for publication Dec. 9, 1958.

* Wonder Base.

Fig. 2.—Fingernails.

were noted in all the nails. The thumbnail and first and second fingernails were involved to a greater degree; whereas the third and fourth fingernails were involved to less degree.

The nails first developed a dull, lustreless appearance, then gradually a greenish-brown discoloration slowly permeated the nail plate. Along the edges and in the middle, opaque white areas appeared. The opaque areas have since gradually become grayish in color, and the nails are developing superficial flaking (Figs. 1 and 2).

Patch tests were performed with the 22 ingredients separately; nail polish, base coat, and cuticle remover. All tests were negative after 48, 72, and 96 hours.

Comment

This patient presents onychodystrophy after the use of an occlusive, nonpermeable base coat. The changes noted were not due to allergic sensitivity but probably to physical and chemical changes. The pigmentation of the nails is similar to that which one sees in persons handling resorcinol. The opaque areas and flaking are probably due to the occlusive effect of the base coat.

104 E. 40th St. (16).

REFERENCES

1. Sulzberger, M. B.; Rein, C. R.; Tanburg, S. J.; Wolf, M.; Shair, H. M.; Papkin, G. L.: Allergic Eczematous Reactions of Nail Bed: Persistent Subungual and Ungual Changes Based on Contact with "Undercoats" Containing Artificial Resins and Rubbers, J. Invest. Dermat. 11:67-72 (July) 1948.

2. Rein, C. R., and Rogin, J. R.: Allergic Eczematous Reactions of Nail Bed Due to "Undercoats," Arch. Dermat. & Syph. 61:971-983 (June) 1950.

Obituaries

LESTER HOLLANDER, M.D.
1891-1959

On February 2, 1959, Dr. Lester Hollander, of Pittsburgh, died suddenly in his office.

Dr. Hollander was born in Hungary, in 1891, and came to this country at an early age. He graduated from the University of Pittsburgh Medical School in 1912 and, for a while, was in general practice. His postgraduate training in Dermatology was obtained in Europe and New York.

He was one of the original founders of the Pittsburgh Skin and Cancer Foundation and, for many years, had been Medical Director of this organization. At one time he served as Associate Professor of Dermatology at the University of Pittsburgh Medical School. He was a Fellow of the American College of Physicians and of the American Academy of Dermatology and Syphilology. Other organizations in which he was active included the American Association

LESTER HOLLANDER, M.D.
1891-1959

for Cancer Research and the International Academy of Medicine. He was head of the Department of Dermatology, Montefiore Hospital, Pittsburgh.

During World War I, he served with the Volunteer Medical Service Corps. During World War II, when many of the staff of the Foundation were in active military service, he daily saw and treated a large portion of the clinic patients in addition to his administrative duties. He regarded this exhaustive schedule as his personal responsibility and as a gesture of friendship to those of us who were overseas.

Dr. Hollander was the author of numerous scientific papers, particularly on clinical dermatology. He was an exceptionally gifted clinician and a superb teacher. During the ten-year period in which residents were trained at the Pittsburgh Skin and Cancer Foundation, he took a direct personal interest in each

of these men and devoted much of his time to individual instruction. In spite of the pressure of a large private practice, he was never too busy to help direct the course of the Foundation and its personnel and that of each resident. Those of us who were so trained will always owe a debt of gratitude to this talented teacher and friend. The thousands of patients he treated at the Foundation and as consultant to the Pittsburgh City Hospital at Mayview will keep his memory alive for years to come.

Dr. Hollander's survivors include his widow, Josephine Parfitt Hollander; a daughter, Mrs. David Tynberg, and a sister, Mrs. Stephanie Buchler.

His family will miss his devoted concern for each of them. His fellow physicians have lost a gifted colleague and Dermatology has lost a distinguished practitioner.

JOSEPH M. SHELTON, M.D.

ANNOUNCEMENTS

Postgraduate Course in Occupational Skin Problems at University of Cincinnati.—The Institute of Industrial Health of the University of Cincinnati announces that the fourth biennial course of instruction in Occupational Skin Problems will be given during the week of Oct. 26-30, 1959. It will be presented by the Department of Preventive Medicine and Industrial Health, University of Cincinnati, in collaboration with the Occupational Health Program of the United States Public Health Service and the Department of Dermatology of the University of Cincinnati.

The program will be divided into daily sessions, consisting of lectures and clinical demonstrations, field instruction in industrial plants, and panel discussions. The didactic presentations will include a review of the anatomy, physiology, and chemistry of the skin. Detailed consideration will be given to the etiology, diagnostic evaluation, and treatment of occupational dermatoses, as well as specific measures for prevention and control of these problems. Current concepts regarding cutaneous cancer, allergic reactions, and medicolegal problems will be discussed.

Physicians interested in attending the course should write for an application blank to the Secretary, Institute of Industrial Health, The Kettering Laboratory, Eden and Bethesda Ave., Cincinnati 19. Early application is advised, since attendance will be limited.

Symposium on Griseofulvin and Dermatomycoses.—The University of Miami School of Medicine, Department of Medicine, announces an International Symposium on Griseofulvin and Dermatomycoses to be held in Miami, Fla., Oct. 26, 27, 1959. All interested physicians and investigators are invited to attend. Further information may be obtained from Dr. Harvey Blank, Professor of Dermatology, Jackson Memorial Hospital, Miami 36, Fla.

Seminars in Dermatology.—The University Extension and the School of Medicine of the University of California at Los Angeles, in cooperation with the Dermatologic Research Foundation of California, Inc., offer advanced seminars in dermatology at the University Residential Conference Center at Lake Arrowhead, Aug. 26 through Aug. 30. Participating in the program will be Drs. Asboe-Hansen, Henry Michelson, Franklin Ashley, surgeon, Carl Pearson, internist, Louis Winer, and Tom Sternberg. Applications for enrollment should be sent to the Department of Continuing Education in Medicine, University of California Medical Center, Los Angeles 24.

The New, Newer, and Newest

From Atlantic City, where meetings were held in June of the American Medical Association, the American Dermatological Association, and the Society for Investigative Dermatology, the welcome news that the A. M. A. Section on Dermatology and the Society for Investigative Dermatology plan to meet concurrently next year, each group to retain its organizational setup. Our appreciation and congratulations to the officers of both groups for working out this new arrangement which should benefit all of us as well as dermatology.

The officers for 1959-1960 are as follows:

For the American Dermatological Association:
Marion Sulzberger, President
Lawrence Beinhauer, Vice-President
Wiley Sams, Secretary

For the Society for Investigative Dermatology:
Tom Fitzpatrick, President
Harvey Blank, Vice-President
Herman Beerman, Secretary

For the A. M. A. Section on Dermatology
Wiley Sams, President
William J. Morginson, Vice-President
Edward Cawley, Secretary
Stanley Huff, in charge of Scientific Exhibits
Winfred Showman, Representative to the House of Delegates

The meetings were well attended and worth while—good papers, good talk, good fellowship. Those who did not attend, thinking that they can read everything later, are deluding themselves. The round-table discussion on corticosteroid therapy at the A. M. A. session, for instance, was the source of a wealth of practical information covering experiences and conjectures of a sort that cannot be transcribed onto paper.

Out of the mouths of dermatologists—

—"Boric acid dressings are staging a comeback."

—"There are two kinds of medical speakers, one brings a message, the other brings slides."

—"I spend five times as much time explaining as I do planing."

—"In urticaria pigmentosa we have not yet scratched the surface."

—"embolized to the skin."

—"To judge from the exhibits this year, the drug houses and the government will be competing for and taking over the scientific exhibit section."

—"Granuloma pyogenicum sure can fool you—always have a microscopic examination."

—" . . . about time we begin to speak of iatrogenic cures."

—"The discussion has brought out more important points than did my paper."

—As Mark Twain said, "One gets such a wholesale return of conjecture from such a trifling investment of fact."

—"Nomenclature should not be too rigid."

—"They are now referring to it as the *remarkable* mast cell."

—"Any similarity between these remarks and the published version will be strictly accidental."

—"Griseofulvin is another nail in our coffin . . . will put us out of business . . . on the contrary, will benefit dermatologists provided they practice proficient mycology . . . will lead to more antibiotics just as penicillin led to a rash . . . works like that invisible shield on television . . . need for cautious watchfulness despite optimistic reports."

—"Acne problem will be solved by endocrinology and genetics."

—"Emotional attitude of the therapist is also important."

—" . . . represents a marriage of fundamental studies and practical experiences."

—" . . . soon may recognize importance of complete physical and laboratory examination of household pets."

—"Burrow's solution is more than 100 years old."

—" . . . about time we fought back and aggressively too [referring to unjustified malpractice suits]."

—" . . . have only seen the beginning of development of synthetic steroid compounds. . . . It is the disease that calls the shots, not the drug. . . . Don't try to play the steroids and don't send a boy to do a man's job. . . . The many illusions to increasing death rate from corticosteroids not valid."

And then there was the extraordinary bathing beauty contest staged by the A. D. A. at this place where beauties most abound.

"The Lake Erie Folie Ayschious," or "The Sorryassiforms at Atlantic City."

1. Introduction—Masher of Cerumenies—Dr. J. Walter Wilson
   (Trying to wax humerus in your ears).
2. Grand Entry of King Neptune —Dr. Fred M. Jacob
   Representing the entire company.
3. "Beauty" Pageant —All contestants.
4. Miss Annie Pruritus —Dr. E. George H. Curtis
   Representing UNO what and UNO where.

5. Miss Vi Tiligo —Dr. William B. Guy
   Representing the loss of what?
6. Miss Sally Varsan —Dr. Leon Goldman
   Representing the good old days.
7. Miss Gracie O'Fulvin —Dr. Thomas Butterworth
   Representing Notta Fungus Amongus.
8. Miss Cutie Sanserina —Dr. Henry Brunsting
   Representing the neglected end.
9. Miss Callie Ahsity —Dr. Lawrence Beinhauer
   Representing the sole of the beat generation.
10. Miss Eckie Moessis —Dr. Roy Kile
    Representing the Reds.
11. Miss Rose Ayschia —Dr. Herman Beerman
    Representing what causes it.
12. Miss Packy O'Nickie —Dr. Herman Pinkus
    Representing the great untrimmed.
13. Grand Finale
    —A remarkable and wonderfully happy production
    "And all that faith creates or love deserves
    Terrible, strange, sublime and beauteous shapes."

H. R.

Announcements

Papers for A. M. A. Section on Dermatology.—Dermatologists and other physicians who may be interested in presenting a scientific paper before the Section on Dermatology of the American Medical Association, which meets in Miami Beach, in June, 1960, are invited to submit the title and a 100- to 150-word abstract of the proposed paper for consideration by the program committee. Abstracts should be sent to the Secretary of the Section on Dermatology, Dr. Edward P. Cawley, University of Virginia Hospital, Charlottesville, Va. The deadline for submission of abstracts is Dec. 1, 1959.

Winner of American Dermatological Association Essay Contest.—Dr. J. Graham Smith Jr., of Miami, Fla., read his prize winning essay on "The Aged Human Sebaceous Gland" at the Seventy-Ninth Annual Meeting of the American Dermatological Association, Inc., at The Claridge Hotel, Atlantic City, N. J., June, 1959. Other prize winners in the annual contest were Dr. James H. Graham, of Philadelphia, and Dr. Elson B. Helwig, of Washington, D. C., "Bowen's Disease and Its Relationship to Systemic Cancer," second prize; Dr. Troy G. Rollins, of Woodland, Calif., "Necrobiosis Lipoidica Diabeticorum and Necrobiosis Lipoidica Granulomatosis," third prize, and Dr. Daphne Anderson Roe, of Wilmington, Dela., "The Psoriatic Process," fourth prize.

Papers for the Tenth Annual Essay Contest should be submitted to the Secretary, Dr. Wiley M. Sams, 308 Ingraham Building, Miami 32, Fla., not later than Nov. 15, 1959.

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

Arthur B. Hyman, M.D., President
Henry Silver, M.D., Secretary

Nov. 20, 1958

Diagnosis: Bowen's Disease of the Penis: Response to Grenz Ray Therapy. Presented by Dr. Earle W. Brauer and Dr. M. Gelfard (by invitation).

A Negro man, now aged 71, was first seen two years ago, at which time he presented an ulcerated and indurated lesion on the penis of eight months' duration. A biopsy specimen at that time showed no evidence of a malignancy. A second biopsy specimen taken two months later was read as "psoriasiform dermatitis." Dark-field studies on the penile lesion were consistently negative, as were also serologic tests for syphilis. A search for Donovan bodies produced doubtful findings. The Frei skin test was positive.

Despite various topical medicaments and systemic antibiotic agents of every type, the lesion failed to respond.

A review of the previous biopsy specimens was then made and intraepidermal epithelioma was revealed.

During the next month, the patient received 6,500 r of grenz radiation (500 r $\times$ 13) with a HVL of 30μ Al.

In the past four months the erosion has progressively resolved, and so at present the patient presents but slight crusting within a large depigmented, atrophic patch.

Discussion

Dr. Edward H. Mandel: I should like to hear about the comparative effectiveness of thorium X and grenz ray in the treatment of this condition.

Dr. Arthur B. Hyman: The alcoholic solution of thorium X would not be practicable because of the discomfort that would be caused by it and the lacquer needed to keep it on; besides, it would be quickly removed.

Dr. Alexander A. Fisher: It can be expected that there will be burning sensation and discomfort when alcoholic solutions of thorium X are applied on lesions which are excoriated or denuded. In such cases I have been advised to use an aqueous solution of thorium X. I wonder if Dr. Brauer could tell us whether aqueous solutions of thorium X are efficacious.

Dr. Earle W. Brauer: In the past I have had occasion to present several cases of Bowen's disease which have responded to grenz-ray therapy. The patient this evening is not being presented as a cure but only to demonstrate how radiosensitive to grenz rays an epithelioma of this type is.

Thorium X can be used in Bowen's disease. I have seen the condition respond very well to this radioactive isotope. However, the alcoholic solution would be very uncomfortable to apply to an eroded penis and a collodion cover would not be too effective, and so much of the thorium X would be lost. As to aqueous solutions of thorium X, they are less certain of calculated effect unless permitted to dry thoroughly and then lacquered in the customary way. Nothing much would be gained in this way. It was for these reasons that grenz-ray therapy was employed in this case.

Diagnosis: Epidermolysis Bullosa (Mostly of the Mucous Membranes) in Identical Twins. Presented by Dr. Helen O. Curth.

Identical twins, 23 years old, present nearly identical complaints and manifestations. They are said to have been delivered normal but, on the second day of life, bled from the tongue and the tips of several fingers. From infancy, it was noted that most finger- and toenails failed to develop (a few are present). Disturbance of hair growth was also noted in childhood. Throughout the years the patients have had recurrent hemorrhagic bullae in the mouth, pharynx, and esophagus. Operations for rectal fissures were undergone by both at the age of 12, and one of the twins underwent esophagoscopy because of hemorrhages, possibly from bullae in the upper alimentary tract.

Examination at this time shows the anonychias, white patches on the buccal mucosae, milia on the tongue, and scars at the sites of bulla around the ankles.

Discussion

Dr. David Bloom: I believe that these are cases of mild dystrophic epidermolysis bullosa. However, there are unusual features which make this diag-

Submitted for publication Jan. 19, 1959.

nosis somewhat uncertain. The absence of finger- and toenails with the history of falling off of the nails soon after birth would bespeak severe dystrophic epidermolysis bullosa, but, in fact, these patients present moderate cutaneous and mucous membrane involvement. The small lesions on the tongue which may correspond to milia seen on the skin are also unusual. One has to think of another possible diagnosis, namely, ectodermal dysplasia involving the nails and associated with a mild form of epidermolysis bullosa. Both of these conditions are inherited. In these cases no ascending family members are affected. We may then be dealing with a mutation in one of the parents resulting in an affected first generation.

Observation of future generations may throw light on the correct diagnosis in these cases.

With respect to the factor of trauma, trauma is indeed an important factor in the production of bullae in the simple type of epidermolysis bullosa. In the severely dystrophic type the underlying factor leading to bulla formation is most probably a more profound metabolic disturbance of unknown nature.

In any event, I should suggest a biopsy of one of the milium-like lesions of the tongue.

DR. ABRAHAM J. ORFUSS: I was impressed with the comparatively slight amount of damage which these twins have sustained from such a destructive disease as epidermolysis bullosa can be. They present no evidence of bulla formation or scarring over the joints and none of the atrophic changes that one usually associates with this condition. On grasping and pressing the hands, I was struck by their soft velvety skin. I also had the impression that the joints were slightly hyperextensible. Is it possible that we might be dealing with a mild manifestation of the Ehlers-Danlos syndrome?

DR. HELEN O. CURTH: These young women seem to show mirror-image qualities, which presumably make them identical twins. When they were small, their resemblance was still greater.

I agree with Dr. Bloom that this is epidermolysis bullosa of the dystrophic type. The presence of milia and scars, the absence of nails, and most of all the pattern of recessive inheritance speak in favor of this type of genodermatosis. I did not see any signs of the Ehlers-Danlos syndrome.

The twins were apparently frequently ill when they were small but have been slowly outgrowing their disorder. I think the number preponderance of hemorrhagic blisters on the mucous membranes over the cutaneous blisters is interesting. The disturbance of the growth of scalp hair may also have been a sign of epidermolysis bullosa. The possibility of epidermolysis bullosa seems to have escaped the specialist who performed the esophagoscopy. This is a rather risky undertaking in patients with epidermolysis bullosa in view of the possible sequelae. I never saw milia on the tongue before. Since milia on the skin in epidermolysis bullosa are supposed to represent obstructed dilated sebaceous glands, it would be nice to know which type of glands are obstructed on the tongue. I suppose biopsy is in order.

Diagnosis: Arsenical Pigmentation with Keratoses of the Palms and Soles, Squamous-Cell Epithelioma of the Palm, and Multiple Superficial Basal-Cell Epitheliomas of the Trunk.
Presented by DR. CONRAD STRITZLER.

A 55-year-old electrician is presented with a generalized, mottled pigmentation of the trunk, keratoses of the palms and soles, an ulcerating lesion of the right palm proven histologically to be a squamous-cell carcinoma, and multiple superficial basal-cell epitheliomas of the trunk. These conditions are now of many years duration but were insidious in onset. During childhood, the patient was told he had chorea, for which drops (Fowler's solution?) were given over a period of many months.

One year ago, a basal-cell epithelioma was excised from the right temple. Six months ago, the large, fungating squamous-cell epithelioma of the right palm was curetted and given 4,500 r x-ray therapy. It has failed to heal. Many superficial flat epitheliomas of various shapes and sizes on the trunk have been excised or curetted. A few such lesions, scattered on the thighs, pubic area, and right foot, are still present. The patient's general health has not as yet been affected.

Discussion

DR. HANS H. BIBERSTEIN: Before discussing arsenotherapy for dermatologic conditions (other than syphilis), I wish to make a few comments on the question of carcinogenesis and arsenic medication.

In this country "superficial flat epithelioma" of the skin is usually ascribed to previous administration of arsenic by many observers. Although there is no doubt that arsenic has cancer-producing ability, I doubt that it should be incriminated in cases of superficial flat epitheliomas to the extent that it is. I doubt it for the following reasons: Medication with arsenic has been widely used in Germany and other parts of Europe for a long time, not only in dermatologic conditions (e. g., psoriasis, lichen planus, dermatitis herpetiformis, mycosis fungoides, warts, hair-fall) but also in general medicine (e. g., anemias of many varieties, lymphoblastomas). Despite this wide use of arsenic, superficial flat epitheliomas were rare in Germany. As a matter of fact, when Arning presented a case of the type we see tonight under the title of "multiple carcinoids of the skin" (*XII. Congr. Dtsch. derm. Ges., Hamburg,* 1921 [*Arch. Dermat. u. Syph.* 138:458, 1922]), prolonged discussion by

Jadassohn, Herxheimer, Zieler, Frieboes, Kyrle, Hoffman, Lewandowsky, Arzt, Ullmann, and Volk followed. Not one of them referred to arsenic as a possible cause, although all of them doubtlessly had vast experience with arsenical medication. One would think that if arsenic were as cancerogenic with respect to superficial flat epithelioma as it is said to be, such epitheliomata would have been nothing unusual in middle Europe and such authorities as those cited would have been aware of a correlation. The simple facts are that the condition in point was rare in Germany, and arsenic was not implicated when the condition was found. I am not sure that I saw as many as 10 cases of it during the more than 15 years (1920-1935) that I worked in the Dermatologic University Hospital in Breslau.

Now we come to the situation here. It seems to be exactly in reverse. Arsenotherapy is sparingly used in this country, and superficial epitheliomata are common. What explains the paradox? If one finds a history of arsenotherapy in a case of superficial epitheliomata, may it not be purely coincidental and not causal, or may it be causal only because the dose was huge or because the period of administration was prolonged beyond a period of time to be considered safe on the basis of past experience? I do not know the answer except to say that, while there is no "law" about dose and duration of treatment with arsenic, no harm came of the Continental practice of administering Fowler's solution (diluted in 2 parts of peppermint water) in ascending doses of 2 to 10 to 20 drops three times daily by mouth (Jadassohn, J.; Dermatologie, Wien, Bern, Weidmann & Co., 1938, pp. 179-180) or 0.1 to 1.0 cc. daily of a 1% solution of arsenous acid by intramuscular or subcutaneous injection. It has been my practice to give these medicaments in a course of 6 weeks for psoriasis and 8 to 10 to 12 weeks for lichen planus, dermatitis herpetiformis, and mycosis fungoides. After such a course, a pause of at least three months should ensue before arsenic is resumed again if necessary.

Of course, arsenic, like nearly every other agent, may have side-effects that will force permanent discontinuance. However, one common reaction, namely diarrhea, requires but temporary discontinuance. After a few days or a week, cautious resumption may result in tolerance.

DR. FRANCES PASCHER: I am impressed with the carcinogenic potentialities of inorganic arsenic. I do not think it is possible to state how much is safe or how long or short a term is permissible. The patients we studied (Pascher, F., and Wolf, J.: *J. A. M. A.* 148:734-736, 1952) were given arsenic for asthma in the form of Fowler's solution for 18-20 months before arsenical hyperpigmentation, arsenical keratoses, and keratoderma appeared. The time of onset for these and other manifestations (e. g., epitheliomatosis) may be as early as 1 month or as late as 30 years after the ingestion or parenteral administration of the drug.

DR. CONRAD STRITZLER: The question of the advisability of using x-ray therapy in treating the squamous-cell cancer of the palm has been raised, with reason. I have seen identical lesions in patients treated with Fowler's solution by the Biloxi Clinic and at first I advised excision and plastic repair. One such patient soon developed widespread metastases. Since then we have been treating these lesions with thorough curettement and x-ray therapy, with better results. This patient, however, has, I believe, a slowly healing painful ulcer marking the site of therapy for the prickle-cell carcinoma.

We have now seen several patients treated years ago (by the Biloxi Clinic) with Fowler's solution for asthma who have developed arsenical pigmentation, keratoses of the palms and soles with prickle-cell epitheliomas. The frequent, almost consistent association of the basal-cell epitheliomas makes it difficult to avoid a belief in the etiologic role of arsenic in this condition.

Diagnosis: Systemic Lupus Erythematosus with Nephrotic Syndrome in a Pregnant Woman.

Presented by DR. FRANCES PASCHER.

A white woman, 31 years old, is now in the beginning of her eighth month of pregnancy. Two previous pregnancies were uneventful, except for pyelitis two years ago, during the second. Four months ago, after some hours in the sun, "blisters" and "pus-pimples" appeared, two of which had to be lanced. A few days later a rash which has spread and has become progressively more marked was noted.

When first seen, one month ago, the patient complained of marked fatigue and she looked acutely ill. A widely disseminated purple-red macular erythematous scaly eruption was found on the trunk, thighs, and upper extremities. The face and lips were puffy and purple-red in color. Two shallow ulcers and a leukokeratotic plaque were found on the buccal mucosa. The feet were edematous. Recorded rectal temperatures taken every four hours for one week showed no elevation.

Laboratory findings were as follows: an L. E. test showed only an occasional L. E. cell; the sedimentation rate was 90 mm. per hour (normal, 15 mm. per hour); the total proteins were 4.9 mg. % (normal, 6-8 mg. %); blood albumin was 1.8 mg. % (normal, 4-5 mg. %); blood globulin was 3.1 mg. % (normal, 2-3 mg. %); the A/G ratio was 0.58 (normal, 1.6-2.0); blood urea nitrogen was 10 mg. % (normal, 10-15 mg. %); blood sugar was 94% (normal 80%-120%); blood cholesterol was 440 mg. % (normal, 250 mg. %); the Wassermann test was negative. Repeated

urinalysis showed 4+ albumin, a few hyaline casts, and red cells on one occasion. Two tests for occult blood in the stool were negative. The hemogram disclosed a leukocytosis of 10,500 WBC, with 75% neutrophils but no anemia. Porphyrins were not demonstrable in the urine.

Treatment was instituted with prednisone in doses of 10 mg. q. i. d. for one week, 10 mg. t. i. d. for a second week, and then 5 mg. t. i. d. Some clinical improvement was noted within 10 days. The patient's weight (146 lb.) and blood pressure 124/88) have remained constant.

Discussion

DR. JULIUS H. POLLOCK: I point out to the presenter the striking similarity of the renal picture in this case to Epstein's nephrosis. The hypercholesteremia is not due to liver damage or to depressed metabolism, but undoubtedly is a compensatory mechanism to maintain osmotic balance in blood by substituting lipids for lost protein. This also happens in Epstein's nephrosis.

Corticosteroids and thyroid should, of course, be used here with care. However, my experience over a period of four years, with almost a dozen cases of gestational dermatoses treated with corticosteroids, has been gratifying. There was striking relief in these most uncomfortable conditions and no harm to mothers and children. This has also been the experience of others who have dealt with dermatoses of pregnancy. I doubt that pregnancy, lupus erythematosus, and nephrosis in any combination is a contraindication to corticosteroid therapy.

DR. EDWARD H. MANDEL: In acute disseminated lupus erythematosus, the combined use of Aralen and corticosteroids has seemed to be more effective than the corticosteroids alone. However, I have not used this combination in a patient with both acute disseminated lupus erythematosus and pregnancy.

I should like to suggest as additional therapy the intramuscular injections of heparinized compatible blood in the amount of 30 cc. three times a week.

DR. ALEXANDER A. FISHER: Dr. Pascher's case reminds me of a Negro woman whom I presented before this Society at the November, 1954, meeting. This woman was 24 years old and was presented because she had lupus erythematosus and chronic nephritis during pregnancy. She had considerable edema of the legs. There was 4+ albumin in the urine and many casts and blood cells. In addition she had a severe secondary anemia. This patient was subsequently treated at the Mt. Sinai Hospital, where she delivered a normal child. After the delivery the lupus erythematosus improved considerably. Although L. E. cells were never found in this patient, it was felt that she was systemic L. E. with chronic nephritis.

As far as the use of steroids in pregnancy is concerned, I wish to state that I have treated several patients with various steroids during pregnancy, and I have been fortunate enough not to have had any ill effects in either mother or child. I recall the trepidation with which I treated my first case of severe herpes gestationis with cortisone. This case was presented at the February, 1953, meeting of our Society and was one of the first cases so treated in New York City. This patient two years later again became pregnant and again had herpes gestationis, which was successfully treated with steroids for the second time without any complications in mother or child.

DR. CONRAD STRITZLER: I take it that Dr. Pascher intends us to understand that the nephrotic syndrome in this patient is a complication of the systemic lupus and not an independent condition.

DR. FRANCES PASCHER: This patient presents an uncommon complication of systemic lupus erythematosus. The diagnosis of nephrotic syndrome was based on the edema, hypoalbuminemia, hypercholesteremia, and massive proteinuria. The inversion of the A/G ratio in this case was due to a drop in the albumin concentration, rather than to an elevation in the globulins which is usually the case with systemic lupus erythematosus. Relatively few instances of systemic lupus erythematosus with nephrotic syndrome have been reported, and as far as I know this is probably one of the first examples in a pregnant woman. She poses a very difficult problem in management.

There is no question that intensive corticosteroid therapy has greatly benefited cases of idiopathic (Epstein's) nephrosis. I am afraid the story in the nephrotic syndrome associated with systemic lupus erythematosus is rather different. Of 10 such cases reported by Belak et al., (*Arthritis & Rheumat.* 1:204, 1958), three developed glomerulonephritis and the other seven died within 3-36 months of the onset of their edema.

One cannot be sanguine about the administration of corticosteroids during pregnancy. Cortisone-induced cleft palate has been reported, (Gluecksohn-Waelsch, S.: Trends in Mammalian Teratology, *Pediatrics* 19:777, 1957). I feel the safest course would be to hospitalize this patient and to administer intensive corticosteroid therapy under close medical supervision.

Case for Diagnosis: Pemphigus Vulgaris? Ocular Pemphigus? Presented by DR. JULIUS H. POLLOCK and DR. IRVING D. EHRENFELD.

Diagnosis: Rosacea-like "Tuberculoid" of Lewandowsky. Presented by DR. FRANCES PASCHER and DR. WILLIAM M. COON (by invitation).

Diagnosis: Porphyria Cutanea Tarda. Presented by DR. JOHN GARB and DR. ALFRED J. SHAPIRO (by invitation).

Case for Diagnosis: Granuloma of Unknown Cause. Presented by DR. ABRAHAM J. ORFUSS.

Diagnosis: Virilizing Syndrome Due to Arrhenoblastoma of Left Ovary? Presented by DR. CONRAD STRITZLER.

Diagnosis: Kaposi's Sarcoma. Presented by DR. ARTHUR B. HYMAN and DR. SAUL BLAU.

Diagnosis: Mycosis Fungoides. Presented by DR. ALFRED W. KOPF and DR. ALFRED J. SHAPIRO (by invitation).

Diagnosis: Facial Granuloma with Eosinophils. Presented by DR. ABRAHAM J. ORFUSS.

Diagnosis: Nevus Flammeus around the Midline of the Face Associated with Epilepsy. (Sturge-Weber Syndrome). Seborrheic Dermatitis of Scalp and Eyebrows. Presented by DR. HELEN O. CURTH.

Diagnosis: Case of Ragweed Dermatitis—Duration Twenty Years. Presented by DR. JULIUS H. POLLOCK.

Diagnosis: Lichenoid Sarcoidosis. Presented by DR. IRWIN I. LUBOWE and DR. EDWARD H. MANDEL.

Jan. 15, 1959

Diagnosis: Allergic Contact-Type Dermatitis Due to Polyethylene.

Presented by DR. ALEXANDER A. FISHER.

A man, aged 34, is a supervisor in a factory where polyethylene tubing and sheets are made from polyethylene pellets. The patient has been working in this factory for six years. One year ago he developed a dermatitis of the hands.

The results of patch testing follow:

Material Tested	Reactions to 1 In. Squares in 48 Hr.	Reactions to Large Sheets in 96 Hr.
1. CA Monsanto clear plastic sheet	+	+++
2. BA Bakelite clear plastic sheet	+	+++
3. BB Bakelite denser plastic sheet	0	
4. 23 A DuPont clear plastic sheet	0	
1. CA Monsanto pellets	+	
2. BA Bakelite pellets	+	
3. BB Bakelite pellets	0	
4. 23 A DuPont pellets	0	

The reactions to the 1 in. squares of the CA Monsanto and the BA Bakelite were mild but definite (1+). The reactions to the pellets may have been caused by pressure. When these same materials were applied to the arms in larger squares and left on for four days, there were markedly positive reactions to them.

It is known that polyethylene molding and extrusion materials are of two types, namely, a general purpose substance that is unmodified but comes with or without colorants and dielectric compounds which contain antioxidants.

The actual sensitizer has not yet been determined. It may be the polyethylene resin itself or a chemical additive. Occasional sensitization to these resins has been reported, especially in workers coating the resins *before* complete polymerization has occurred. However, allergic sensitization to the *finished* product, such as demonstrated in this patient, is apparently extremely rare.

These resins are used in the form of blown bottles, tubing, gloves, tape, sheeting, film, and for packaging, tableware, wire and cable insulation, molded closures, etc.

Submitted for publication Feb. 25, 1959.

Discussion

DR. MORRIS LEIDER: The interpretation of the clinical and laboratory aspects of this case are arguable. Examining the hands, what one sees does not look like allergic eczematous contact dermatitis—the picture is that of a few healing vesicles on the interdigital surfaces of a few fingers. It is what would ordinarily be called pompholyx.

Now as to the patch tests. Performed in ordinary manner of placing the suspect material on the skin under occlusion for two days, a 1+ reaction was obtained. Occlusion of a large area of the skin with a large sheet of the material for four days gave a much severer reaction. It is assumed then that both reactions were truly allergic and that the intensity of reaction was a function of duration of contact. It may well be that both reactions are not in the nature of allergy but rather inflammatory changes in the nature of prickly heat or secondary infection caused by occlusion of the skin with heremetically sealing materials. When one tests with a sealing material like plastic, one is somewhat in the position of testing with an unknown that requires simultaneous control tests on several non-exposed persons in order to see if primary irritancy or some other reaction mechanism, aside from the allergic, is not provoked by them. In this case the patch tests of both 48 and 96 hours of contact and with small and large samples would have been more meaningful if they had been done at the same time on "normal" persons and no reactions had been obtained in the latter.

Failing this control, biopsy specimens of the severe reaction ought to have been done if the

matter were to be presented as proved. Allergic eczematous reactions are in distinctive ways different from primary irritant, secondary infective, or prickly heat-like reactions.

DR. ALEXANDER A. FISHER: As we have indicated in the protocol, allergic dermatitis due to polyethylene must be extremely rare. The medical director of the Union Carbide Corporation, which is the largest producer of polyethylene, has notified me that he is not aware of any cases of sensitization to finished polyethylene and that none of the employees engaged in the manufacture or handling of polyethylene has become sensitized.

Dr. Leider has pointed out that the eruption on this patient's hands does not look like contact dermatitis. This is a valid objection, and we intend to have the patient wear polyethylene gloves for several days to see whether a more typical type of contact dermatitis will develop.

The reason for leaving on large pieces of polyethylene sheeting for more than 48 hours was to make more evident a sensitivity which is of a low degree. Schwartz has pointed out (Schwartz, Tulipan, and Birmingham: "Occupational Diseases of the Skin," Ed. 3, Philadelphia, Lea & Febiger, 1947, p. 67) that in testing with fabrics or with other substances in which the allergen is of a low concentration, large samples of the material may be left on from two to five days.

Dr. Leider's suggestion that a histologic examination be made of the areas where reactions to the polyethylene patch tests were performed in order to determine whether we are dealing with a true allergic eczematous reaction or not is of considerable interest. However, we have recently been studying this problem and have found that such histologic examinations are frequently not very rewarding in differentiating primary irritant reactions from true allergic ones. Many histopathologists, including Dr. Arthur Hyman, concur with this opinion.

Diagnosis: Lichenoid Eruption Due to Color Developer. Presented by DR. ARTHUR B. HYMAN and DR. ROBERT A. BERGER (by invitation).

A 20-year-old Negro youth has been employed for the past two years by a photographic supply house. In the course of his work, he handles at least six different compounds in preparing developer solutions from powders and solvents. He states that the protective clothing worn is inadequate to prevent occasional skin contact with these chemicals. Moreover, the atmosphere is always dusty from airborne powder particles. A skin eruption was first noted by the patient six months ago, beginning with tiny papules on the left forearm. Other areas, as noted below, were progressively involved during the following months. At no time was the eruption eczematous in character. The penile lesions are moderately pruritic; otherwise the condition is asymptomatic. Three other employees in the same plant, all of Pureto Rican extraction, developed similar eruptions. We have observed gradual resolution of the papular elements, although the patient has continued on the job and has not taken special precautions. Therapy has consisted of simple antipruritic creams and oral antihistamines.

When first seen, four months ago, the patient displayed an extensive papular eruption, morphologically typical of lichen planus. Pinhead-sized, round or polygonal, slightly elevated, shiny, erythematous, nonscaly papules were found on the forearms, wrists, and dorsa of the hands. On the penile shaft and the scrotum, the lesions were aggregated into irregular, grayish, lichenified plaques. On the upper arms, eyelids, and trunk, occasional discrete papules were observed with a short linear streak of lesions on the left side of the abdomen (Koebner phenomenon). The eyelid lesions were circinate in outline. In addition, well-demarcated, nummular, hyperpigmented macules were present on the forearms and the right upper eyelid. In the four months during which the patient has been under observation, there has been definite resolution of most of the papules, but the penile lesions and the hyperpigmented macules are little changed. No oral lesions have been seen at any time.

Patch tests gave positive reactions to two of the compounds handled by the patient, namely, to monobenzylparaminophenol hydrochloride and 4-amino-3-methyl-*N*-diethyl-aniline. Neither of these gave primary irritant reactions in the concentration employed (2%) when tested on a control group. The second chemical, the trade name of which is CD_2, is one of a large group, the *p*-amino-*N*-dialkyl-anilines, members of which have been implicated in all the similar cases previously reported. The patient also showed a 48-hour eczematous response to 2% paraphenylenediamine. None of the reactions has evolved into a lichenoid lesion; each shows only hyperpigmentation as a residual effect.

Biopsy revealed the following findings: The horny and granular layers are well formed. The epidermis is irregular. The rete pegs are elongated particularly at their tips, and the basal margins are washed out. This is due to a heavy inflammatory infiltrate which is fairly limited to the papillae and upper cutis. It consists almost entirely of small round cells mixed with a considerable number of melanophages. The picture is strikingly like that of lichen planus.

Discussion

DR. EDWARD H. MANDEL: I have seen approximately 10 patients with this type of eruption; all of them had come in contact with CD_2, which is one of the chemicals comprising a color de-

veloper. In the majority of cases, typical lichen planus lesions were present. However, there were several cases where the cutaneous response was eczematous.

CD_2 is a substituted paraphenylenediamine. The patients in my series were tested with both paraphenylenediamine and CD_2. The patch tests were positive to both and eczematous in character.

This eruption differs from lichen planus in its rather prompt resolution with topical therapy of steroids, compresses, and soft x-ray.

DR. JULIUS H. POLLOCK: As Dr. Hyman states, this is a peculiar eruption to conceive as a contact dermatitis. How can one visualize a distribution like this from contact when it involves the volar aspects of wrists and forearms and then skips to the penis? I believe the eruption is lichen planus and that it may be due to the chemicals cited which are absorbed from the skin or absorbed from mucous membranes after ingestion or inhalation. This part of the mechanism is like that of many drug eruptions.

DR. FRANZ HERRMANN: The fact that drugs can precipitate not only eruptions similar to lichen planus but, also true lichen planus with all its clinical and histological features was likewise in earlier periods subjected to serious reasoning as regards the possible pathogenesis of this dermatosis. Such drugs include Atabrine and, in particular, arsenicals.

DR. ARTHUR B. HYMAN: Clinically and histologically, this case is classic and typical lichen planus. Perhaps one may say that here we have lichen planus of known cause. The patch test reaction to the material used in color developer was that of allergic eczematous contact type dermatitis, not that of lichen planus. The offending material, therefore, most likely produced the lichenoid response, either by inhalation or perhaps by transepidermal absorption rather than by direct contact.

If, as Dr. Herrmann says, the arsephenamines and Atabrine produce exactly the same lesions as seen here tonight, one might seek something in common between these drugs and the color developer in an attempt to find the common denominator for lichen planus in general.

DR. ALEXANDER A. FISHER: In none of the cases of lichenoid eruption due to color developer have lesions of the oral mucosa been described. We are attempting to produce lesions in this area by local applications of the color developer to the mucous membranes of the mouth.

It is interesting to note that this patient also reacts to paraphenylenediamine. In our studies with ordinary paraphenylenediamine we have never seen any relationship between paraphenylenediamine sensitivity and lichen planus. However, there is no doubt in my mind that the substituted paraphenylenediamine which is used in color developer has a definite relationship to the production of a lichen planus-like eruption. It is my belief that the mechanism of the production of the eruption is by contact rather than by inhalation of the color developer, since there have been occasional reports where an eczematous patch test reaction to the substance became lichenoid.

DR. ROBERT A. BERGER (by invitation): The first mention of this unusual phenomenon was by Dr. William R. Buckley of Rochester (A. M. A. ARCH. DERMAT. 78:454 (Oct) 1958). He described the evolution of clinically and histopathologically typical lichen planus lesions from eczematous patch test reactions to certain color-developer compounds. No such evolution was observed in our patient, who showed only a subacute eczematous response to patch testing without the subsequent development of lichenoid papules.

The possibility of systemic absorption of the chemical, with a lichenoid eruption developing in susceptible persons analogous to that seen after the use of quinacrine and arsenicals, was not mentioned by Buckley. The 4-amino-3-methyl-*N*-diethyl-aniline, implicated in our case, is a rather coarse and granular power not likely to be inhaled. However, sufficient quantities might be absorbed through the skin, or through ingestion, to cause an eruption. Certainly the distribution of the lichen planus-like eruption, and the small size and sharp demarcation of the individual papules, suggest some other mechanism than a peculiar contact dermatitis. We then must explain the regular observation of eczematous patch test reactions to color developers in these cases. It may be that this is coincidental, the 4-amino-*N*-dialkyl-anilines having been shown to be strong epidermal sensitizers in guinea pigs, or it may be that the development of eczematous sensitivity of the usual kind enchances absorption of the chemical through the skin, sufficient for the subsequent lichenoid eruption to occur.

Enough such cases have now been observed, as noted by the previous speakers, to rule out one possibility at least—we are surely not dealing with unrelated cases of "idiopathic" lichen planus in color-developer handlers, for the eruption has been seen too frequently, by several different observers. The problem merits further investigation and research.

Diagnosis: Sarcoidosis with Hypertrophy of the Lacrimal Glands. Presented by DR. CONRAD STRITZLER and DR. JAMES MORRELL (by invitation).

A Negro housewife, age 25, is presented with a history of a papular and nodular eruption about the eyelids, forehead, and knees of several years' duration. These lesions have been asymptomatic. There has been an occasional nonproductive cough but no other pulmonary symptoms.

Fig. 1.—Clinical aspect of sarcoidosis about the eyes. Note the papules on the upper lids particularly, and note with special care the enlarged lacrimal glands faintly delineated over the eyeballs at the outer canthi.

The nodules about the lids are soft, smooth, skin-colored, and bead-sized. The nodules about the knees are orange-colored, pea-sized, and fewer in number than those about the lids. There has been significant adenopathy of the cervical, occipital, epitrochlear, axillary, and inguinal lymph nodes, but in recent months these have tended to diminish in size.

The lacrimal glands are enlarged; the eyes are otherwise normal. The spleen is palpable about 1 fingerbreadth beneath the costal margin; it is smooth, firm, and not tender. No other organ edges are palpable. Peripheral nerves are not thickened. A neurological survey is negative.

Laboratory studies were as follows: X-rays of the lungs show pulmonary sarcoidosis. X-rays of the hands, feet, and nasal bones are negative. A Kveim test performed in May, 1958, was positive. Tuberculin tests were negative in 1:10,000 dilution, plus-minus in 1:1,000 dilution. Blood and urine studies were negative. Biopsy specimen from a nodule on the knee showed naked, epithelioid tubercules diagnostic of sarcoidosis.

There has been no response to iproniazid (Marsalid) or chloroquine and little response to a two-month course of prednisone.

The patient is one of four in a series of seven with sarcoidosis who have lacrimal gland hypertrophy. The case is presented to emphasize the frequency and diagnostic significance of this finding.

Discussion

DR. MORRIS LEIDER: Dr. Hyman urges me to open a discussion on the cause of sarcoidosis. At the moment the spirit is as unwilling as the flesh is weak. I should only say that all the evidence that has been adduced to suggest that sarcoidosis is related to beryllium-rich soil or emanations from pine forests is not nearly as strong as the old evidence that sarcoidosis is a rare consequence of infection with organisms like the mycobacteria, some protozoa, and some fungi, at a stage of late immunobiologic developments toward such organisms.

DR. HELEN O. CURTH: I wonder if the involvement of the lacrimal glands has resulted from extension of the cutaneous process, since in this patient the eyelids are severely involved.

DR. JAMES FRANCIS MORRELL (by invitation): From our recent observations, enlargement of the lacrimal glands in sarcoidosis is of far commoner occurrence than we previously were aware. In many cases the enlargement is apparent without even everting the lid. Once we started routinely to look for this sign, we were surprised at the frequency with which we found it. It should be noted that all these cases had concomitant skin lesions of sarcoidosis.

DR. CONARD STRITZLER: It has been difficult to obtain information from ophthalmologists and ophthalmological texts regarding the average size of the normal anterior lobe of the lacrimal gland. Accordingly, we have measured this in 10 apparently normal people. The lacrimal gland is easily visualized by everting the upper lid and having the patient look downward and nasally, wherewith it presents as a yellowish-white, ovoid or globoid, lobulated mass, from 4-5 mm. in diameter.

We have arbitrarily doubled this figure and taken 1 cm. as the upper limit of normal. Using this as our criterion of hypertrophy, we have found four of the seven sarcoid patients in our series with hypertrophy of these glands. None of the patients had other eye conditions found in sarcoidosis, such as uveitis, and none had associated enlargement of the parotids.

This patient's lacrimal glands are 1.5 cm. in their longest diameter and 1 cm. in the least and present as red, oval, granular masses when the lids are everted and the eyes turned downward and nasally.

It may be, of course, that our high incidence of lacrimal gland hypertrophy in these 7 cases of sarcoidosis is purely fortuitous and the next 20 patients we see will show glands of average dimensions. We hope that all clinicians who read this will look for this sign and report to us, so that we can determine its incidence and possible importance as a diagnostic criterion of sarcoidosis.

DR. JOHN GARB: If Dr. Stritzler considers the condition of his patient with sarcoidosis serious enough, and since the patient did not respond to Marsalid, chloroquine and prednisone, I should like to recommend experimental treatment with edathamil disodium. Rukavina, Orkin, and Lynch (*J. Invest. Dermat.* 31:259-262 [Nov.] 1958) reported clinical and histologic evidence of improve-

ment in three cases of cutaneous and suggestive visceral sarcoidosis so treated. At any rate, this form of therapy should be considered in other cases of sarcoidosis that do not respond to whatever we have been using in recent years.

Diagnosis: Reticulum-Cell Sarcoma. Presented by Dr. Max Wolf.

A 56-year-old Italian man presents a tumorous process on various parts of the body of 20 years' duration. The first tumors appeared on the right chest wall and enlarged gradually. Later, more tumors developed on the abdomen, right thigh, and buttocks. Most of the masses grew for two to three years and then underwent partial or complete resolution by scarring. No treatment was given at any time.

Examination five months ago showed on the right side of the chest above the nipple, a globular mass measuring 4×3½ in. in largest and smallest diameters, centrally depressed, traversed by telangiectasias and resembling a keloid in its rubbery consistency. On the outer aspect of the right thigh there was a tumefaction measuring 7×8 in., which consisted of discrete and confluent plum-sized, violaceous, lobulated, hard tumors with indentations between them. To the left of the umbilicus there was a more erythematous process that looked and felt deep and, moreover, showed exudation and crusting on its surface. On the upper left quadrant of the abdominal wall there were several half-dollar and larger sized irregularly shaped atrophic areas. On the posterior aspect of the right thigh there was an atrophic scar that measured 2×4 in. and was the former site of large tumors. To the right of the intergluteal cleft there was a plaque of small palm size that was partly clear in the center and ranged with nodular infiltrations around its periphery. On the left buttock there was a dollar-sized atrophic, wrinkled area. Below the right clavicle there was an erythematous, flat, hard, infiltrated plaque with satellite nodules.

Reexamination at this time revealed intensification of the process in the form of increase in size and number of tumors on the right thigh. The scarring remained as before. In some places superficial bullae have developed on some of the masses, apparently from overexposure to ultraviolet light which has recently been given.

Laboratory studies with respect to the peripheral blood and determinations of total protein, albumin,

Fig. 2.—Clinical aspect of reticulum-cell sarcoma with self-healing tendency.

globulin, and cholesterol yielded normal findings. The sedimentation rate was normal. Serologic tests for syphilis and urinalysis were negative. X-ray examination of the chest showed healed and arrested tuberculous infiltration of both upper lobes. The bones of the hands were normal.

Biopsy was interpreted by Dr. Arthur Hyman as follows: The epidermis is stretched. The uppermost cutis is hardly affected. The rest of the cutis shows a massive infiltrate between the collagen elements, which are rather well preserved. The infiltrate consists of cells of all shapes and sizes, with poorly defined outlines, light-pink reticulated cytoplasm, reticulated nuclei, many mitotic figures, and an admixture of lymphocytic elements and a few polymorphonuclear leukocytes. From a purely histologic point of view this is more like a lymphoblastoma of the reticulum-cell sarcoma type, rather than a granuloma.

No treatment has been undergone except self-administered ultraviolet light with a carbon arc lamp two to three times weekly for the past year upon the advice of a "specialist."

Discussion

DR. FRANCIS PASCHER: The first diagnosis that occurred to me, I must admit, was dermatofibrosarcoma. In view of the histologic findings I have no doubt that we are dealing with a case of reticulum-cell sarcoma. The size, distribution, and configuration of the tumor masses are identical with those seen in a case of reticulum-cell sarcoma presented by Dr. John Garb (A. M. A. ARCH. DERMAT. 71:531, 1955) before this society a number of times. Complete involution with secondary atrophy of some of the lesions is, I believe, a unique feature. We have learned that reticulum-cell sarcoma is not necessarily a rapidly fatal disease. Some patients have been known to survive as long as 20 or more years after the onset.

DR. ARTHUR B. HYMAN: The sections show a massive infiltrate of reticulum type cells, showing variety of shape and size, and among them are many mitotic figures. Therefore, the picture is that of a malignant lymphoma of the reticulum-cell sarcoma type. The two unusual features of this case are (1) the long duration of the disease and (2) the apparent spontaneous disappearance of lesions through the years. The diagnosis is, nevertheless, as stated.

DR. JOHN GARB: The histologic interpretation confirms the clinical diagnosis of reticulum-cell sarcoma, and this case resembles the one I presented before this society (Garb, J.: Reticulum-Cell Sarcoma, A. M. A. ARCH. DERMAT. 71:531, [Oct.] 1955), as noted by Dr. Pascher. My patient lived for 12 years after the diagnosis of reticulum-cell sarcoma was made. The duration of the disease in Dr. Wolf's patient is probably the longest on record. The average duration of life is about four years after discovery of the condition.

DR. MAX WOLF: The clinical diagnosis in this case was rather uncertain because the tumor formation started about 20 years ago. The general health of the patient has not been affected up to now, and many of the tumors, lasting for two to three years, disappeared spontaneously without any special treatment. The biopsy, however, to which the patient finally agreed, established unequivocally the diagnosis of reticulum-cell sarcoma. Similar cases have been reported in the literature (Director, W., and Kern, A.: Reticulum-Cell Sarcoma, *Arch. Dermat. & Syph.* 62:69 [July] 1950; Sonck, C. E.: Primary Reticulum-Cell Sarcomatosis of the Skin, *Acta Dermat.-venereol.* 37: 129-139, 1957), but none of the cases in the literature presented a self-healing tendency of the tumors. The long duration of the disease in our case is also an unusual feature.

Diagnosis: Hemolytic Anemia Following Diasone Therapy for Dermatitis Herpetiformis. Presented by DR. FRANCES PASCHER.

Diagnosis: Circumscribed Keratoderma of the Soles. Presented by DR. JOHN GARB.

Diagnosis: Lupus Erythematosus? Light Eruption? Presented by DR. FREDERICK REISS.

Diagnosis: Atrophoderma (Type?) Presented by DR. ERNST M. ROSENBAUM.

Diagnosis: Pili Torti. Presented by DR. EARLE W. BRAUER.

Diagnosis: Ulcer of a Foot (Artifact?, Functional Vasoconstricting Peripheral Vascular Disease?, Fixed Drug Eruption?) Presented by DR. HANS H. BIBERSTEIN and DR. NATHAN PENSLEY (by invitation).

Diagnosis: Urticaria Pigmentosa with Subcutaneous Lesions Resembling Granuloma Telangiectaticum. Presented by DR. ALEXANDER A. FISHER.

Diagnosis: Porphyria Cutanea Tarda with Sclerodermoid Lesions. Presented by DR. JOHN GARB and DR. ALFRED J. SHAPIRO (by invitation).

Diagnosis: Leiomyoma Cutis. Presented by DR. FREDERICK REISS.

DETROIT DERMATOLOGICAL SOCIETY

George B. Sexton, M.D., London, Ont., Canada, President
Alice E. Palmer, M.D., Secretary
Robert E. Burns, M.D., Recorder

Nov. 12, 1958

Xanthomatous Biliary Cirrhosis Resulting from Thorazine Administration. Presented by Dr. A. C. Curtis and staff.

History.—A 48-year-old white woman was well until Sept., 1957, when, three days after a two-week course of Thorazine therapy for an emotional depression, she noted progressive jaundice and the development of xanthoma. Her course included extreme weight loss, malaise, and increasing jaundice, and xanthomata until two months ago. Since that time, the jaundice has lessened considerably.

Physical Examination.—Xanthelasma palpebrarum, xanthoma of extremities, palms, gingivae, anterior fauces, and eardrums.

Laboratory Findings (August, 1958).—Liver biopsy: intrahepatic biliary obstruction consistent with xanthomatous biliary cirrhosis. Serum bilirubin: 9-11 mg. %. Alkaline phosphatase: 70+ KA units. Serum lipids: total cholesterol, 2,288 mg. %, 9% present as esters; phospholipids, 4,080 mg. %; triglycerides, 54 mg. %; total lipids, 6,566 mg. % (serum clear).

Discussion

Dr. Frederick Kingery, Ann Arbor, Mich. (by invitation): The clinical picture initially was that of typical Thorazine jaundice, except that it progressed. The total serum lipids were over 5,000 mg. %, yet the serum was clear. The serum cholesterol was 2,300 mg. %; phospholipids were 400 mg. %, and the neutral fat fraction was completely normal. This is typical of xanthomatous biliary cirrhosis and is backed up by liver biopsy and other studies.

There is one report in the literature of xanthomatous biliary cirrhosis which resulted from Thorazine administration, and Dr. Bolt, from the Department of Medicine at this hospital, has another case, making a total of three. The only difference between this and the xanthomatous biliary cirrhosis you read about in standard texts is that these patients seem to recover. The importance in this case is in recognizing the fact that Thorazine can produce this kind of picture, even though rarely, and the prognosis may be slightly different than that in true xanthomatous biliary cirrhosis of the idiopathic variety.

The turbidity of the serum depends primarily on the amount of neutral fat in the serum. This is associated with the larger and lower density lipoproteins more than the cholesterol and phospholipids. In this patient the serum neutral fat fraction was normal, and in the patient with essential hyperlipemia, the neutral fat was grossly abnormal and elevated. I think the reason her serum was not turbid was that she had normal serum neutral fat.

Dr. James Rogin, Detroit: It is interesting that this woman has a twin brother who is a chronic alcoholic and who has xanthelasma lesions of the eyelids.

Dermatomyositis. Presented by Dr. A. C. Curtis and staff.

Discussion

Dr. Arthur Curtis, Ann Arbor, Mich.: These are two cases of dermatomysitis; one is an adult, and one is a young girl. The adult is presented for several reasons. If one has had the opportunity, as we have here, to study this disease in fairly large numbers, one is also impressed by the fact that perhaps other than slight elevation of the sedimentation rate, the laboratory examination is negative. This man is 35 years old, and an acute upper respiratory infection and pneumonia brought him to this hospital. He presented several things I had not seen before in dermatomyositis. There was evidence of nephritis, changes in his serum proteins, and a rather striking leukocytosis, all of which one usually does not find in this disease. The question, of course, arises whether the nephritis and leukocytosis and upper respiratory infection with pneumonia are due to the same thing. He was placed on steroids, which he is still receiving. The idea was if we could keep him alive for a period of one to two years, the chances were he would pass into an inactive stage of his disease. There was no evidence of neoplasm in his examination.

The girl was 14 years old. In a study which Dr. Everett and I published, we found that in none of the children was there evidence of a neoplasia as an etiological factor. In the adult it was found in about 18%. Likewise in children, when the onset is associated with regurgitation of fluid or food that prognosis is much worse than in that group where that particular symptom is absent. The girl had regurgitation of liquid, particularly in the early days of her illness. She says that is now better. Dermatomyositis is a progressive disease, and once it runs its course it ends with about 50% mortality, about 25% being disabled and about 25%

Submitted for publication Feb. 7, 1959.

of them having a fairly normal but somewhat atrophic telangectatic skin as an end-finding. Of the people who recover from dermatomyositis, about half will eventually develop an extensive calcinosis. Those that live and whose disease becomes inactive might be treated with disodium edathamil if calcinosis occurs.

DR. CLARENCE LIVINGOOD, Detroit: In the adult, did you notice any difference in therapeutic effect with triamcinolone and prednisolone?

DR. ARTHUR CURTIS, Ann Arbor, Mich.: No, I do not think so because when he first came in he was on prednisolone and an extremely ill person. In fact, we thought he was going to die. He then began to improve. I can not tell when he was switched to triamcinolone or that muscle weakness, which is part of this disease, has been greater on the latter drug.

DR. RICHARD HARRELL, Ann Arbor, Mich.: I think if anything the man has done better on prednisolone than triamcinolone, but it was given in larger doses, so it is difficult to compare the effect.

DR. CLARENCE LIVINGOOD, Detroit: Theoretically, it might be better not to use triamcinolone because of its well-known muscle-weakening effect.

Blue Nevus. Presented by DR. A. C. CURTIS and staff.

History.—A 10-week-old white boy has had an extensive macular, slate-blue colored nevus on the right leg and foot, present since birth. Pregnancy and labor were normal. Growth of the nevus has been proportional to that of the extremity. There has been no evidence of malignancy or irritation.

Cutaneous Examination.—There is a 13 cm. slate-blue macular lesion on the dorsum of the right leg and foot. No biopsy was permitted.

Blue Nevus Arising During Pregnancy. Presented by DR. A. C. CURTIS and staff.

History.—In May, 1958, a dark stain appeared on the dorsum of the right wrist which the patient thought was caused by her wrist watch. At that time, this 22-year-old white woman was seven months pregnant. The lesion increased in size and thickness until she was seen by the presenter, in June, 1958.

Radical surgery had been recommended, but the attending dermatologist resisted this pressure when he was assured by the pathologist that the lesion was benign. The pregnancy was terminated by cesarean section within two weeks of the calculated date of delivery.

Cutaneous Examination.—There is a lesion on the dorsum of the right wrist 4×5 cm. in diameter. It is blue-black in color, with many small, hard nodules in it.

Laboratory Findings.—Not contributory.

Biopsy.—Blue nevus.

Treatment.—None.

DR. STANLEY JOYCE, Detroit: The findings in both cases fit better into a diagnosis of Mongolian spot; the baby an extrasacral and the young woman an aberrant type. Both patients show a light bluish, flat patch, and not a discrete papulonodule of a blue nevus. In either case, the characteristic cell is histologically similar; i. e., spindle-shaped, bipolar cells containing melanin granules, located in the dermis and separated from the epidermis. The difference of density of these cells account for the thickening of blue nevus and its lack in Mongolian spots. There may be an extrasacral or an aberrant Mongolian spot with or without a sacral lesion. The infant's spot could be expected to fade gradually within four years, except that a few may continue until teen age.

The ancestors of the infant are central European and those of the young woman Armenian. Mongolian spots are more frequent in Oriental races.

The question of a Mongolian spot appearing as a consequence of pregnancy, as possible in the second case, is an interesting one. I am not familiar with the relationship or with any such association which has been reported.

DR. ARTHUR CURTIS, Ann Arbor, Mich.: One of the reasons why this woman was shown with the dermal nevus on the arm was that it appeared with pregnancy. Lerner has shown there is an increase of melanin-stimulating hormone (MSH) during pregnancy. By injecting MSH into patients, he was able to develop new nevi in a short period of time. This large area of dermal pigment occurred about the 6th month of pregnancy. These were pigmented junctional nevi, and he was afraid that if he continued the MSH they might become malignant. At Memorial Hospital pregnancy is often the cause of malignant melanoma.

DR. LEO MEIDLER, Ann Arbor, Mich. (by invitation): I should like to ask Dr. Pinkus if it is possible histopathologically or without the usually special stains to differentiate the blue nevus from Mongolian spots or from a nevus-cell nevus?

DR. HERMANN PINKUS: As Dr. Joyce pointed out, a blue nevus is a relatively small, well-circumscribed papular lesion, while a Mongolian spot is a large macule or irregular area without visible or palpable infiltration. Histologically, the blue nevus shows many of the characteristic stellate or fusiform dermal melanocytes in fairly close arrangement, sometimes mixed with melanophages and fibrocytes. In a Mongolian spot, these cells are widely scattered in otherwise normal skin; one often has to look hard to see them in hematoxylin and eosin sections. I feel the baby has a rather typical extrasacral Mongolian spot, not a blue nevus. The other case is very unusual in two respects. The lesion is said to have started in pregnancy, and it was papulonodular in the beginning. Today, I could not feel any infiltration;

there was nothing but a macular discoloration of the skin. However, the clinical history suggests that this case is atypical and can not be pigeonholed as either a blue nevus or a Mongolian spot.

DR. ARTHUR CURTIS, Ann Arbor, Mich.: The woman says that this nevus, or pigmented spot, has improved since her delivery.

DR. HERMANN PINKUS, Monroe: The world literature contains a number of studies concerning the incidence of sacral pigmented spots in various races. Larsen and Godfrey (*Am. J. Phys. Anthropol.* 10:253-274, 1927) working in Hawaii concluded that the sacral spot is a universal human character but is vestigial and rudimentary in Western Europeans. Its occurrence segregates in crossbreeding in a ratio that fits a two-factor hypothesis. There seems to be a dominant gene for pigment and recessive determining gene. Maxia, (*Monitore zool. ital.* 56:300, 1948) who found the spot in 13% of babies in southern Sardinia, also favors a multifactor inheritance. Bahrawi (*Arch. Dermat. u. Syph.* 141:1922) found the characteristic cells on histologic examination of sacral skin even in European infants who had no clinical pigmentation. Otherwise, sacral spots have been reported as regularly occurring in the natives of Turkey, Angola, South Africa, Viet-Nam, East India (Bengali), Java, and Colombia, to quote a few recent investigations. North American Negro infants show sacral spots regularly, and often there is extensive pigmentation of large areas of the back.

Cases presented by DR. ARTHUR C. CURTIS and staff of the University Hospital, Ann Arbor, Mich.

Localized Myxedema (2 cases).
Fox Fordyce Disease.
Lupus Erythematosus—Chronic Discoid.
Candidiasis of Skin.
Scleroderma—Acrosclerotic with Raynaud's Phenomenon (2 cases).
Lichen Sclerosis et Atrophicus.
Multiple Leiomyomata.
Xanthoma Tuberosum and Essential Hyperlipemia.

Case for Diagnosis: Ulcers of Leg.

Case for Diagnosis. Presented by DR. EUGENE HAND, Saginaw, Mich.

Localized Scleroderma in Father and Daughter. Presented by DR. GEORGE B. SEXTON, London, Ont., Canada.

Papers presented.

Dietary Fat in Essential Hyperlipemia: A Metabolic Study. Presented by DR. F. A. J. KINGERY.

Fox-Fordyce Disease: Report of a Case, with Histochemical and Endocrinological Study. Presented by DR. LEOPOLDO MONTES.

Chemical Nature of Mucopolysaccharides in Pretibial Myxedema. Presented by DR. WILLIAM BIERWALTES.

LOS ANGELES DERMATOLOGICAL SOCIETY

Floralou Kettenbach, M.D., President
Jerome K. Fisher, M.D., Secretary

Oct. 8, 1958

Cylindroma (Turban Tumors). Presented by DR. S. W. BECKER and (by invitation) DR. A. BERMAN.

This 44-year-old white man developed four tumors on the scalp at the age of 27. They were called "wens" by his local physician and were excised. He remained free of lesions for approximately two years when, while in New Guinea, new tumors appeared on the scalp and rapidly enlarged. Since then, many new lesions have developed. According to the patient, new lesions continue to appear and existing tumors continue to enlarge.

The patient states he has had dengue fever (1942) and malaria (1945). In 1943, a thyroglossal duct cyst was excised. A vasectomy was performed in 1957.

No similar lesions of the scalp are known to have occurred in other members of the family, although a 30-year-old brother has "a few little tumors" in the perinasal folds.

The significant physical findings are confined to the scalp and perinasal areas.

The patient was presented to the Tumor Board at the Long Beach VA Hospital. The Board recommended a trial of radiation therapy to an isolated lesion to attempt to evaluate the radiosensitivity of the tumors.

An isolated lesion on the left suboccipt was selected and was treated over a period of two weeks with a total dose of 4,500 r (air). Factors: 120 kv., 3 mm. al filter, HVL 2.8 mm. al. At the conclusion of treatment the tumor was softer and flatter.

Discussion

DR. LOUIS H. WINER: The onset of this condition in a patient at age 30 years is a bit late in life. The histologic section showing the X-radiation caused a disappearance of cells forming the tumor is also unusual for an epidermal hamartoma. One should do a reticulum stain on tumors of this type, because not infrequently reticulum-cell sarcoma may histologically resemble a cyl-

Submitted for publication Dec. 31, 1958.

indroma in the scalp. These are very readily differentiated by the reticulum stain, showing a large amount of fibers in the reticulum-cell sarcoma and very little in the cylindroma.

DR. ANKER K. JENSEN: I believe that these tumors of the scalp could be removed with a post-cautery. I saw patient with a similar condition that had been treated with Mohs' technique, and the results were good. I also feel that a plastic surgeon could remove these lesions and follow up with skin grafts.

DR. S. W. BECKER (Close): Our pathologist thought it was a cylindroma. Dr. Keasbey, consultant on the Tumor Board who has studied sweat gland tumors especially, thought it was a cylindroma. The surgeon said that he could go down to the galea aponeurotica and remove all the tumor and then apply a graft. Dr. Craig, consultant in x-ray therapy, said that he thought that roentgen therapy did improve these tumors. For that reason, the roentgen therapist treated one tumor, causing considerable shrinkage of the tumor cells. I think my own preference would be for plastic surgery.

Erythema Multiforme Bullosum. Presented by DR. S. W. BECKER and (by invitation) DR. WILLIAM B. REED.

This 39-year-old wife of a college professor developed at 16 a reaction to a vaccination which was called an eczematoid dermatitis. She had no previous history of allergy, except slight urticaria to strawberries. In January, 1955, the patient was vaccinated again in preparation for a trip to South Africa. On route to South Africa she developed first on the vaccinated arm and then on the rest of the extremities an urticarial reaction. Upon arriving in South Africa, she was hospitalized for two months. She was given phenobarbital and diphenhydramine (Benadryl) with development of severe blistering. Dermatitis herpetiformis was suspected, and she was given sulfonamide with more blister formation. She was then given prednisone, 30 mg. q. d., with development of epigastric distress. The medication was abruptly stopped with disappearance of all lesions. She remained clear until November, 1955, when she had a few bullae. In January, 1956, she again developed a flare of erythema multiforme. Finally, she went to the Mayo Clinic in the summer of 1956 for hospitalization of one and one-half months.

On therapy of Roniacol and corticotropin (ACTH) she continued to have blisters—some as large as 12 cm. in diameter. She was given prednisone with an ulcer regimen. Her course was still stormy, and finally she was discharged on prednisone, 20 mg. q. d. She was sent to Dr. J. Walter Wilson. She cleared for nearly one and one-half years, until she developed an abscessed tooth which required acetylsalicylic acid and removal with procaine anesthesia. She started to get a recurrence on her arms and legs. Flare-ups as noted before were always at time of menstruation.

She was seen by Dr. Reed (presenter) on Sept. 8, 1958, with early bullous lesions of erythema multiforme and given a high dosage of prednisone (40 mg.) which was lowered rapidly in two weeks. She cleared until dosage was lowered to 0.5 mg. At this time, she started to become more physically active with school teaching. Flare-up has occurred on the trunk, with the older lesions on arms and legs clearing (Sept. 30, 1958). She is now on a dosage of prednisone, 5 mg. q. d.

Biopsy shows the picture of erythema multiforme with considerable eosinophilia in the infiltrate around the vessels. Patient showed at Mayo a persistent blood eosinophilia of 5%-10%. Ear, nose, throat, and pelvic examinations were negative. Stool examination was also negative. No focus of infection was found, nor was a duodenal ulcer demonstrated.

Discussion

DR. DANIEL J. PERRY: I agree with the diagnosis presented and can only speak in generalities about the problem of bullous erythema multiforme. This patient clearly illustrates what we all recognize, namely, that we are dealing with a reaction pattern which can be precipitated by many agents and factors. Her past history suggests that she has a propensity for other cutaneous reactions, since she has also had episodes of urticaria and eczematous dermatitis. Thus far, each of her recurrences of erythema multiforme appear to be related to a specific and different trigger factor. The question of vaccines producing this disease has recently been reemphasized by a case report wherein erythema multiforme followed both the first and second injections of Salk vaccine. The causative factor in the vaccine was not determined. Since many agents can apparently produce erythema multiforme, it seems that the answer lies in some systemic or metabolic abnormality. Continuing studies should be made of their physiological, biochemical, and neurophysiological status.

DR. NORMAN E. LEVAN: This case is reminiscent of a group which, while resembling in many respects erythema multiforme and in others dermatitis herpetiformis, has features which distinguish it from either. I have seen several such; Dr. Eugene Farber, at Stanford, has had a number, and we have had occasion to study two in collaboration.

Most of the patients have been women, in whom the condition first appeared in adult life, persisting for long periods of severe involvement, with

remissions of varying duration. Although the cutaneous surfaces are often widely involved, mucous membrane lesions are either absent or few and equivocal. The lesions range from blebs, arising usually on a slightly erythematous basis, to more polymorphic plaques with erythema, crusting, and, at times, urticarial components. These plaques may be rather arciform. More than one type of lesion may be present simultaneously. Pruritus is almost always intense. Histological examination shows, as in tonight's sections, large numbers of eosinophils in the dermis and, when blebs are present, in their contents.

Unlike erythema multiforme, this condition responds very poorly and incompletely to steroid therapy, except that itching may be partially alleviated. Sulfapyridine is without effect. The best responses seem to be obtained by a combination of steroids and widespread antibiotics administered for prolonged periods. Hence, although in the cases seen no specific sources of infection could be demonstrated, and there was no elevation of antistreptolysin titers, the question of cryptic focal infections as etiologic factors could not be completely excluded.

Until the uncovering of specific etiology allows for more definitive classification, it may be well to consider these cases as a more or less distinct group deserving an approach differing, as discussed, from that applicable to other members of either the erythema multiforme or dermatitis herpetiformis groups.

Dr. Samuel Ayres Jr.: Apparently, her first attack was triggered by a smallpox vaccination, which brings to mind one or more cases reported by Dr. Nelson Paul Anderson of erythema multiforme having been triggered by herpes simplex. Then she said she was free for a year and a half and the second episode was not triggered by anything that she can recall and continued for quite some time. She said she was then free for nearly two years. The present attack followed the extraction of an abscessed tooth. Perhaps it does represent a bacterial allergy, and there may be some chronic focus somewhere that is not apparent. Occasionally, abnormal intestinal bacteria can be present without causing diarrhea or G. I. symptoms. I should second Dr. Levan's method, of using a broad-spectrum antibiotic. I think any case of long, drawn-out erythema multiforme—or any case of chronic urticaria, which, of course, is a first cousin, deserves the trial with broad-spectrum antibiotics for a couple of weeks. I have seen several instances of rather striking results following its use.

Louis H. Winer: Histologically, the section from this patient showed hyalinization of the vessel walls, perivascular infiltrate of lymphocytes with a few dispersed eosinophils and edematous changes in the collagen around the vessels. These findings are compatible with a diagnosis of allergic angiitis which is frequently seen in drug eruptions.

Dr. A. Fletcher Hall: I now have a patient in the hospital with a clinical picture identical to this woman's, only about 10 times as severe, with edema, erythroderma, and fever, due to meprobamate, a drug which many of us prescribe rather freely. It is too bad that we do not have something as definite to blame in this case, but I think we recognize an erythema multiforme as a pattern reaction, like headache, arthritis, diarrhea, or the many other clinical states that can be caused by a great variety of etiological agents. I think that the search should go on in this case because there must be some pattern that the various clues can fit into to make a reasonable background for this case. I presented a case, very similar to this, about 10 years ago, in a woman, approximately the same age, who was also a school teacher. It was the consensus of the Society that it was a drug eruption, but drug ingestion was very well ruled out. She turned out to have Hodgkin's disease, of which she died.

Dr. J. Walter Wilson: I never reached any conclusion as to the drug cause of her eruption. I was surprised to see her tonight with such severe recurrence, but only the tiniest amount of one of a number of medicaments is needed to produce an eruption of this type—a surprisingly small amount will often suffice. Many times, therefore, it is almost hopeless to find the actual cause. In a patient of mine with a tattoo, the red portion of the tattoo became irritated because he had received one injection of polio vaccine which contained Merthiolate 1:10,000. The actual amount of mercury received can be calculated to be approximately 0.025 mg. He reacted in the identical manner when he received a subsequent injection of the same material. Thus, we must respect what an acetylsalicylic acid tablet (containing as it does some 12,000 times as much drug) could do to an extremely sensitive person.

Dr. Murray Zimmerman: I wondered whether the γ-globulin level had been checked. I am interested because I have a similar patient and Dr. Foster told me that he had had such a patient who cleared on γ-globulin.

Epstein wrote up cases of penicillin urticarias that went on for years without known penicillin reexposure. He put these patients on milk restriction, and they cleared—some as much as one and a half years later. This case was ostensibly from one injection of penicillin. Dr. Marvin Knoll found the first reaction from polio vaccine. It was inconceivable to me that ten units of penicillin could give anyone a chronic allergic reaction. However, after Doctor Knoll's case, I found and proved seven cases (*J. A. M. A.* 167:1807-1809

[Aug. 9] 1958) of severe penicillin reactions from this very small amount (about 10-20 units) of penicillin. There was a report in A. M. A. ARCH. DERMAT., January, 1959, on penicillin urticarias from dairy products. We have had four well proved cases where the penicillin ingested in milk caused a severe allergic reaction, including one case with erythema multiforme, as striking as this patient. I mention this only to show that even if you think you are taking a good history, you may be missing something like penicillin-contaminated dairy products. As another example, there is even an azo dye in orange peel to color the orange peel. Since we have no concept of how many drugs people are exposed to, they certainly have no notion themselves.

DR. WILLIAM B. REED (Close): I appreciate the discussion. Her history is very complicated, but one thing is known. She is extremely sensitive to many medications. While hospitalized at Rochester, she developed tremendous-sized bullae on her body after I. V. corticotropin (ACTH). She was clear for nearly one and a half years without any medication, but with the appearance of an abscessed tooth, she took acetylsalicylic acid. This is probably the cause of the present flare-up. She gets flares during her menstrual periods, and I believe also that chronic nervous exhaustion has played a large part. On bed rest she has definitely improved. For this patient, the fewer drugs used, the better she will be.

Nevus Unius Lateris Versus Lichen Striatus. Presented by DR. LAURENCE J. UNDERWOOD.

Linear Nevus. Presented by DR. IRVING A. LEWE (by invitation) and DR. MAXIMILIAN E. OBERMAYER.

Lymphocytoma Cutis? Presented by DR. SAMUEL AYRES JR. and DR. SAMUEL AYRES III.

Case Presented for Diagnosis: (Nonspecific Allergic Eczema)? Neurodermatitis? Presented by DR. MURRAY C. ZIMMERMAN.

Presented for Diagnosis: Not a Keratoacanthoma Nor a Carcinoma. Presented by DR. CLEMENT E. COUNTER.

Pityriasis Rubra Pilaris (Lichen Ruber Acuminatus). Presented by DR. MURRAY C. ZIMMERMAN.

Hemorrhagic Sarcoma of Kaposi's. Presented by DR. ANKER K. JENSEN.

Nov. 12, 1958

Pigmented Purpuric Lichenoid Dermatitis (Gougerot and Blum). Presented by DR. PAUL D. FOSTER.

Multiple Idiopathic Hemorrhagic Sarcoma (Kaposi), Associated with Lymphosarcoma of Supraclavicular Node, and Ductal Carcinoma of Breast. Presented by DR. BEN A. NEWMAN and DR. S. J. TASKER (by invitation).

Widespread Discoid Lupus Erythematosus with Circinate Lesion. Presented by DR. GORDON MACDONALD.

Nevoxanthoendothelioma. Presented by DR. NORMAN E. LEVAN.

Submitted for publication Dec. 31, 1958.

Case for Diagnosis. Presented by DR. ANKER K. JENSEN.

Patch Testing to Various Steroids. Presented by DR. WALTER F. SCHWARTZ.

Case for Diagnosis: Penicillin Reaction? Presented by DR. ROBERT L. DAY.

Pityriasis Rubra Pilaris. Presented by DR. S. WILLIAM BECKER and (by invitation) DR. JOSEPH W. PIDGEN.

Scleroderma (Morphea): Appearing While Taking Cortisone. Presented by DR. CHARLES G. STEFFEN.

Case for Diagnosis. Presented by DR. JOHN R. MUNGER and DR. DONALD G. LINDSAY.

Keratoacanthoma. Presented by DR. MAXIMILIAN E. OBERMAYER.

MANHATTAN DERMATOLOGICAL SOCIETY

Perry Sachs, M.D., President

Maurice J. Costello, M.D., Secretary

Oct. 14, 1958

Ichthyosis Vulgaris. Presented by DR. ANTHONY C. CIPOLLARO.

A girl, now aged 6½ years, was first seen at the age of 5 days covered with a generalized bullous eruption. A diagnosis of epidermolysis bullosa hereditaria was suggested at that time. The eruption responded well to polysporin ointment and calamine lotion. With the clearing of this initial eruption and over the past six years the skin has remained scaly, dry, and erythematous. The child has developed normally in all other aspects. There

Submitted for publication March 9, 1959.

is no family history of significance except that the father has hay fever.

The entire integument is dry, tightened, shiny, and scaly, with a slightly erythematous hue.

The patient has received small doses of thyroid extract. Locally, 1% salicylic acid in various ointment bases has been used. For the past four years the process has seemed to be stabilized, resembling ichthyosis.

Discussion

DR. M. J. COSTELLO: I agree with the diagnosis of ichthyosis vulgaris. I also think this dermatologic care is responsible for the survival of the child who was very sick in the beginning. We have used 10% salt in Aquaphor, the salt first dissolved in water and then mixed with Aquaphor. It would be worth while trying at this stage.

DR. GEORGE M. LEWIS: Does Dr. Cipollaro consider in retrospect that the early bullous lesions were part of the ichthyosiform disease, or did they represent infection?

DR. JACK WOLF: We do not often have the opportunity to see the cutaneous manifestations which precede the development of ichthyosis vulgaris so well demonstrated as they have been tonight. However, I find it difficult to establish a relationship between ichthyosiform congenital erythroderma and ichthyosis vulgaris. I think the two are essentially different clinical pictures without any relationship.

DR. NATHAN SOBEL: I agree with Dr. Wolf. I think it is now ordinary ichthyosis. Incontinentia pigmenti, which is also a nevoid condition, also is known to start with bullae. The Scandinavians have been using salt baths in the treatment of ichthyosis for many years.

DR. ADRIAN BRODEY: I had the privilege of following this case at the beginning with Dr. Cipollaro. I do not think there was any question at that time that this was the congenital erythrodermic bullous form of ichthyosis.

DR. A. C. CIPOLLARO: The purpose of presenting this case is to show the evolution of the disease. Very few of us have had an opportunity to see a child at the age of five days. I saw her in consultation with the pediatrician and obstetrician, and the condition was horrible. It was a bullous eruption at that time, and we talked about Reiter's disease, pemphigus, epidermolysis bullosa, syphilis, and other conditions. The obstetrician assured me that when the baby came out of the birth canal she had these lesions, and there had been no appreciable change when I saw her. There was intense erythema, exfoliation, and bullous lesions, particularly on the palms and soles. I do not believe there was any secondary infection. She was in an incubator, which might have influenced the temperature. If you had seen the child at birth I think many of you would have agreed with me that the diagnosis was epidermolysis bullosa hereditaria. Later, I changed the diagnosis to erythroderma ichthyosiforme congenitale; and now, at the age of 6½ years, the girl presents typical lesions of ichthyosis vulgaris. Based on only one case which I have observed for four and one-half years I have come to believe that erythroderma ichthyosiforme congenitale is a transient stage of ichthyosis vulgaris. If we knew nothing about the past history of this child, I think we should all make a diagnosis of ichthyosis. I am grateful for the suggestion of using 10% salt solution. I have got such good results by letting her soak in plain water and then using salicylic acid ointment that I am disinclined to change. I do not know whether thyroid helps this condition, but I have given it along with baths and salicylic acid ointment in strengths of 1% to 3%.

Melanoma of the Penis. Presented by DR. ORLANDO CANIZARES.

A man, aged 62 years, has had black lesions on the penis for as long as he can remember. He noted an ulceration of the glans about six months ago.

There is an ulceration of the glans penis about 8 mm. in diameter. The borders are soft and slightly raised. There are several slightly keratotic black lesions next to the ulcer. There is no inguinal adenopathy.

Biopsy specimens revealed a thick, edematous epidermal layer, and some sections contained aggregates of cells which were evidently somewhat melaniferous. In most sections there was an infiltration of large cellular elements which had large, deeply staining nuclei. In many of the sections there were cells which contained much pigment, most of which appeared to be melanin and some of which suggested hemosiderin. Were it not for the tumor cells in the epidermis a diagnosis of reticulum-cell sarcoma might be considered. However, in view of all the changes present, the diagnosis must be melanoblastoma (Dr. G. F. Machacek).

Discussion

DR. NATHAN SOBEL: Is the histology considered malignant? I understand there is some controversy among pathologists on individual cases concerning the exact criteria to make a diagnosis of malignancy.

DR. WILBERT SACHS: No dissection can make a 100% diagnosis. There are always cases that are borderline, but in general there is no difficulty in stating whether the lesion is benign or malignant. I think I gave the criteria clearly in my paper (*J. A. M. A.* 135:216-218 [Sept. 27] 1947).

Were there or were there not theques? If there are theques, I have said that it is a malignant melanoma. We must assume that the pigment within the tumor cells, in the epithelium, is melanin and that it is, therefore, nevocarcinoma.

DR. A. C. CIPOLLARO: If we had seen this man at 30 years of age, we would probably have made a diagnosis of junction nevus. Should we have been justified in amputating the penis on the basis of a diagnosis of a junctional nevus and on the basis of preventing a melanoma from developing at the site of a nevus? The removal of the nevus would have been justified without grossly mutilating the penis. The patient now has a melanoma. Shall an amputation of the penis be advised in the absence of enlarged inguinal nodes? I should be inclined to remove the local lesion and save as much of the penis as possible.

DR. WILBERT SACHS: If it were known to be a junction nevus, that could have been removed with little or no deformity and no amputation would have been necessary.

DR. ADRIAN BRODEY: I most heartily agree with Dr. Cipollaro. Even at this age the patient would be miserable with an amputation. If one is going to amputate, one might as well do a radical groin dissection. The patient would have a rather stormy postoperative course and a terrific psychologic adjustment to make. I also feel that local excision should be done. In spite of the pathologic report, we do not know just how malignant the lesion is. With a local excision the patient may live out his years.

DR. J. ABEL (by invitation): A neurologist told me of two patients who committed suicide after amputation.

DR. WILBERT SACHS: If this turns out to be an early nevocarcinoma and it were removed by peripheral biopsy, we should have a guide to further therapy. It it were advanced, I should do nothing because nothing will save the patient's life. A local excision should work very well if the lesion is early; few, if any, patients with advanced lesions have lived.

DR. M. J. COSTELLO: The clinical picture of this lesion suggests to my mind lentigo maligna, or malignant freckle of Hutchinson. In these lesions there is a play of color from honey to brown and finally to jet black. When the last change occurs, the lesion is thought to be a malignant melanoma. I have presented some of these cases at these meetings; all the patients are alive, though most of them have been called malignant melanoma. Dr. Weidman in one case called it malignant melanoma of utmost malignancy. Certainly, this case should be treated conservatively because the lesion will outlive the man.

DR. A. C. CIPOLLARO: It takes more courage to advise removal of the lesion than to advise amputation of the penis. Admittedly the risk is greater, but, on the other hand, the patient is saved from a severe emotional crisis which might conceivably lead to suicide.

DR. GEORGE M. LEWIS: We have a responsibility to the patient who comes to us to present a conservative approach. If the lesion is histologically malignant, is accessible, and can be locally excised, that should be done. If, on the other hand, it has ulcerated and there are already hematogenous metastases, even heroic or mutilating therapy is of no avail. In this instance, the advisable therapy would seem to be local excision. Is there a statistical improvement in the cure rate from mutilating surgery? In the last series that I saw, this was not apparent.

DR. JACK WOLF: I agree with Dr. Costello's opinion that the lesion resembles a melanotic freckle. Nevertheless, I think the lesion should be removed. The Mohs technique would offer the best approach in that the exact extent of the lesion could be determined, and no more than the necessary amount of tissue removed. We owe the patient adequate removal, whether the lesion is a melanotic freckle or not. Even if the lesion proved to be a malignant melanoma, I should certainly object to amputation of the penis. There is sufficient statistical evidence to show that as much is achieved with adequate local excision as with a mutilating operation. We have discussed this so often among ourselves that, as a group, I think we are unanimous in believing that adequate excision is indicated and that mutilating operations add to the misery of life without prolonging it. I saw one such example in the office two days ago: metastatic melanocarcinoma after extensive removal two years previously.

DR. PAUL GROSS: Miescher has obtained good results with caustic doses of contact x-ray therapy, but that may not be indicated in this case. One might consider a lymph node dissection first, and if histologic examination is negative, then local excision may be sufficient.

DR. PERRY SACHS: Lymph node dissection is a radical procedure. In view of the fact that metastases of melanocarcinomas are so wide and unpredictable and spread equally if not more by the blood stream than by the lymphatic system, I think just local excision is indicated.

DR. ORLANDO CANIZARES: This case has been a problem and a great responsibility. I was hoping that you would suggest a conservative approach and am gratified that the majority feel that way. I shall present these views to the patient and go along with conservative therapy.

Lymphoma Cutis. Presented by DR. JULES E. VANDOW.

A Case for Diagnosis (Hailey-Hailey Disease of the Mouth?) Presented by DR. JOHN W. DOUGHERTY.

Reticulum-Cell Sarcoma. Presented by DR. NATHAN SOBEL.

Eczema Keratoticum (Occupational), Refractory to Therapy. Presented by Dr. M. J. Costello.

A Case for Diagnosis: (Subacute Disseminated Lupus Erythematosus? Pemphigus Erythematosus?). Presented by Dr. Adrian Brodey.

Poikiloderma (Civatte). Presented by Dr. George M. Lewis.

Delusions of Parasitosis. Presented by Dr. A. C. Cipollaro.

A Case for Diagnosis: (Dermatitis Herpetiformis?). Presented by Dr. Orlando Canizares.

A Case for Diagnosis: (Light Sensitivity Dermatosis? Hailey-Hailey Disease?). Presented by Dr. Nathan Sobel.

METROPOLITAN DERMATOLOGICAL SOCIETY OF NEW YORK

Wilbur B. Hurlbut, M.D., President

Herbert J. Spoor, M.D., Secretary

Oct. 16, 1958

Idiopathic Atrophoderma of Pasini-Pierini. Presented by Dr. Charles F. Post.

The patient is a 33-year-old white male schoolteacher. The eruption on the right posterior chest appeared spontaneously about one year ago. Within the past three months, more areas with deeper pigmentation have appeared. There are no subjective symptoms.

History.—The past history shows that he had the usual childhood diseases and, in addition, scarlet fever and pneumonia. At the age of 10 years, he had idiopathic purpura, which lasted for three weeks. The patient has had no serious injuries but has had the following operations: tonsillectomy and adenoidectomy, 1938; hernia repair, 1943; hemorrhoidectomy, 1950. The father and mother, in their sixth decade, are in good health. The patient has two brothers who are also in good health. There is no family history of any similar skin trouble or allergies. The patient teaches an agriculture course at a New Jersey high school. He has never been outside the United States.

A complete systemic review is negative, except for an intermittent low back pain that is presumably caused by a slipped intervertebral disk.

Examination.—Along the somatic distribution of the lower left posterior costal area, lumbar area, there are slightly depressed, slightly scaly brownish pigmented areas that vary in size from a pea to the largest, which measures 3×5 cm. All the areas are irregularly shaped, and some appear to be confluent. The central portion of the largest 3×5 cm. area shows a small, firm, white scar. None of the other areas shows scarring that is evident to the naked eye or palpation.

Laboratory Biopsy.—Sections of a specimen of skin from the "back" reveal an epidermis which shows for the most part hyperpigmentation, although there appears to be a small area of relative depigmentation. The basal layer appears to be composed of hydropic cells. There is present a large cystic hair follicle which is surrounded by fibrosis and a chronic inflammatory reaction. The rest of the cutis is relatively normal, showing but a slight perivascular infiltration in its upper strata. Several other hair follicles show some evidence of a chronic perifolliculitis. As far as I know, the pathology of cutaneous papillomatosis and Pasini-Pierini atrophoderma is extremely slight and indefinite. I should like more information on the case and should be glad to study this problem further. I have seen at least one typical instance where there were large areas of hyper- and hypopigmentation with an almost occult atrophoderma, a case of Pasini-Pierini.

Course and Treatment.—The patient has been observed for two months, during which time there has been very little change in the appearance of the eruption. No treatment has been given.

Discussion

Dr. Baker: The zoster-like arrangement gave me the impression of a nevus.

Dr. Domonkos: I agree with the diagnosis. We have followed two patients with this disease on the arms and legs. One patient, whom we have had under observation for at least six years, has done remarkably well. We do not know whether or not it is due to the medication, but she has taken chloroquine (Aralen), one tablet a day, for several years, and the lesions have become lighter and, perhaps, a little bit less depressed.

Dr. Sloane: He now shows a residual scleroderma which has not yet "burned out."

Dr. Post: This year, the first comprehensive article concerning this disease appeared in the American literature (Canizares, O., et al.: A. M. A. Arch. Dermat. 77:42 [Jan.] 1958). Italian and South American dermatologists have exhibited a continuing interest in this dermatosis for 25 years. Dr. V. Torres, one of Dr. Canizares' co-authors, first called this to our attention at Columbia-Presbyterian Medical Center. We have been able to recognize one or two cases at the clinic, and this case comes from my private practice.

Submitted for publication Dec. 1, 1958.

The zosteriform distribution is typical. The literature states that the atrophic areas show bluish pigmentation. This patient shows only brown pigmentation, possibly because he got a good sun tan this summer.

For 20 to 30 years, cases of this type have been presented at various dermatologic societies throughout the United States. The diagnosis of morphea has always been discussed, but most men have commented that they did not know exactly how to classify this cutaneous atrophy. Since the publication of Dr. Canizares' article, the disease should be recognized more readily.

Tinea Barbae Caused by T. Purpureum. Presented by DR. ROYAL M. MONTGOMERY.

A white man, aged 50 years, has had the present eruption for five weeks. He works as an elevator operator. He is also a diabetic and is taking two tolbutamide (Orinase) tablets daily and is on a restricted diet.

He was first seen on Sept. 30, 1958.

At that time, there was a boggy, sharply limited tumor about 1½ in. in diameter in the center of the right cheek. Many follicular pustules were present in the area, with some erythema extending over the cheek toward the nose. Temperature was normal. There were also mottled red scaling patches in the groins and in the intergluteal area. The soles were red and scaly. Some toenails were dystrophic and yellow.

Laboratory Examination.—Wood's light examination, positive.

Culture from Cheek.—Trichophyton purpureum.

Therapy.—Previous therapy, penicillin, and erythromycin, without results.

The patient was treated with solid carbon dioxide (Dry Ice) and 10% salicylic acid ointment. There was 75% improvement in two weeks.

DR. MILLER: I had one patient with this infection on the face who responded to salicylic acid in alcohol. It took three months for complete recovery. No other treatment was used. Trichophyton rubrum infection is not as difficult to treat on the face as it is elsewhere.

DR. SPOOR: It would be interesting to know whether it is the same organism strain in the groin as was on the face. The likelihood is that it is, but I think that the point should be checked.

DR. HURLBUT: This is certainly an interesting case. It is almost identical with the one Dr. Montgomery showed us a year or so ago. Dr. Michelson saw that patient and stated that, in his experience, T. purpureum infection of the beard was rare.

DR. MONTGOMERY: The man whom Dr. Hurlbut was talking about was not improving until Dr. Michelson saw him and suggested using solid carbon dioxide and strong salicylic acid ointment. Today, he is fine. This man was started on the same regimen. He has been on this treatment, actually, only two weeks.

Nevus Comedonicus. Presented by DR. MILTON B. SLOANE.

Hemangioma Cavernosum; Arteriovenous Fistula? Presented by DR. ANTHONY N. DOMONKOS.

Epidermolysis Bullosa. Presented by DR. MILTON B. SLOANE.

Lichen Planus of the Oral Mucous Membrane and Chronic Gingivitis. Presented by DR. ALEX A. YOUNG JR.

Dermatitis Herpetiformis? Prurigo Nodularis? Presented by DR. A. W. YOUNG JR.

Granuloma Annulare. Presented by DR. THOMAS N. GRAHAM.

Mycosis Fungoides? Presented by DR. MILTON B. SLOANE.

Dermatitis: Etiology? Presented by DR. HERBERT J. SPOOR.

Infected Steatocystoma Multiplex. Presented by DR. WILBUR B. HURLBUT.

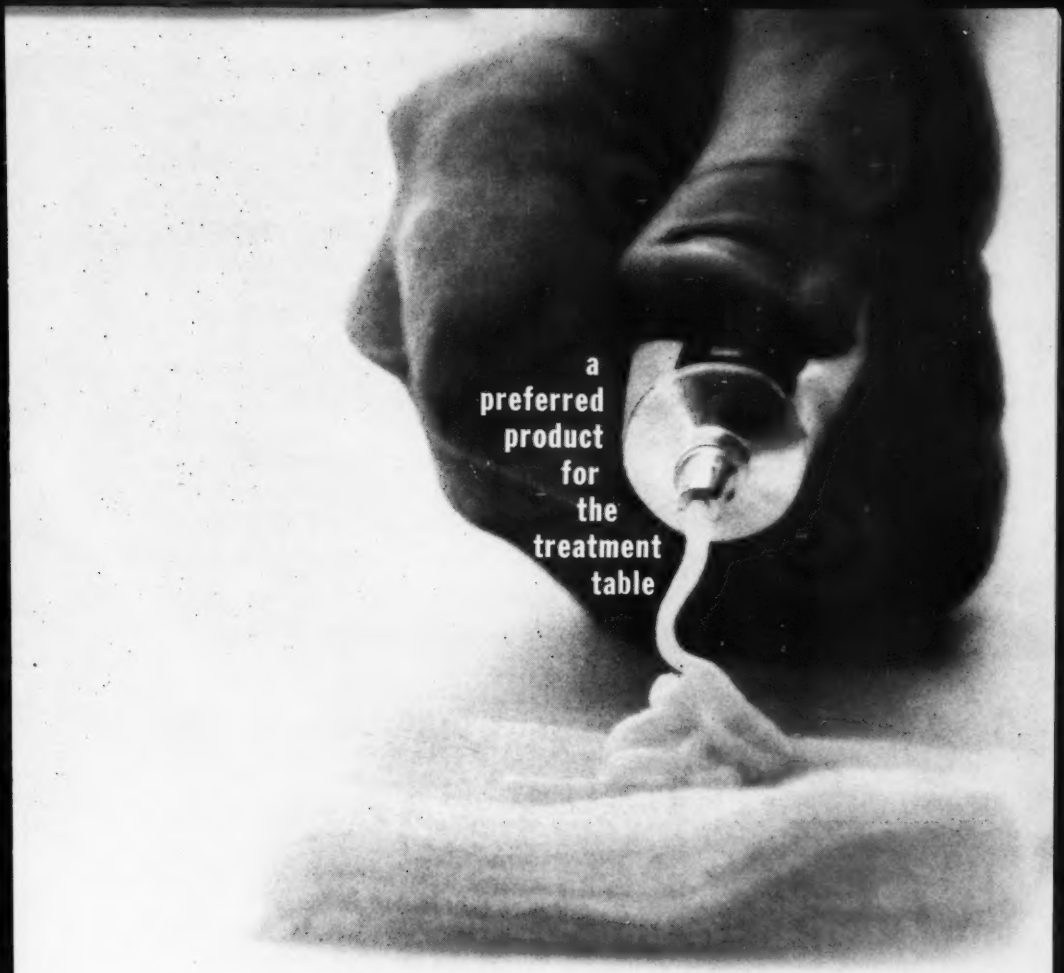
Books

Il Cancro Cutaneo: Gli Epiteliomi (Skin Cancer: The Epitheliomata) (in Italian). By I. Bosco, M. Binazzi, A. Tosti, E. Marchini, and R. Scerrato. Price, 12,000 lira. Pp. 1,115. N. Simonelli, Perugia, 1956.

The size of the book is impressive for a subject somewhat limited; 1,115 pages, of which 114 are devoted to 5,172 references. It has 182 black-and-white illustrations and 15 excellent color plates printed on an effective hyperglossy paper. Bosco, head of the Dermatologic Clinic of the University of Palermo, and his pupils present the result of evaluating an enormous quantity of clinical material and of original experimental work. A first section is devoted to history; relation of cancer to dermatoses, to environment, and to the terrain; the problem of precancer; malignity, and the general clinical and biological aspects. A special section is devoted to the clinical aspects, the cytology and cytodiagnostic aspects, and the etiopathogenesis. Nuclei and cytoplasm of normal and cancer cells are object of a detailed investigation. An original line of study is the allergoimmunitary reactivity of tumors in general and of skin cancer in particular.

With the contribution of eighteen university dermatologic clinics, twelve large dermatologic hospital services, and several pathology, radiology, and gynecology institutions through Italy, valuable clinicostatistical data are gathered. Statistics from all over the world are also given.

The book represents an important contribution to dermatology and to the field of cancer in general.



because Neo-Polycin Ointment

helps clear topical infections promptly

Neo-Polycin® provides neomycin, bacitracin and polymyxin, three antibiotics preferred for topical use because this combination is effective against the *entire* range of bacteria causing most topical infections...has a low index of sensitivity...and averts the risk of sensitization to lifesaving antibiotics, since these agents are rarely used systemically. And Neo-Polycin provides these three antibiotics in the unique Fuzene® (polyethylene glycol diester) base, which releases higher antibiotic concentrations than is possible with grease-base ointments.

Each gram of Neo-Polycin contains 3 mg. of neomycin, 400 units of bacitracin and 8000 units of polymyxin B sulfate in the unique Fuzene base. Supplied in 15 Gm. tubes

PITMAN-MOORE COMPANY, DIVISION OF ALLIED LABORATORIES, INC., INDIANAPOLIS 6, INDIANA

The
1-2-3 Treatment
for
Warm
Weather
Dermatoses

Poison ivy, poison oak, insect bites, Anogenital eczema, athlete's foot, superficial mycoses, Acute and subacute contact and allergic dermatitis.

Samples and literature on request

1 ACUTE STAGE
DOMEBORO® pH 4.2
Cool Wet Dressings

2 POST TREATMENT
ACID MANTLE®
Creme pH 4.2 • Lotion pH 4.5

3 FOR DESTROYING FUNGI
QUATRASAL®
Fungicidal Spray

DOME Chemicals Inc.
THE MOST TRUSTED NAME IN DERMATOLOGICALS
NEW YORK 23 • LOS ANGELES 46 • In Canada: 2765 Bates Rd., Montreal

1. DOMEBORO (Burow's Solution)
2. ACID MANTLE (aluminum acetate in specially formulated bases)
3. QUATRASAL (salicylanilide, trimethyl octadecyl ammonium pentachlorophenate, and isopropl alcohol 94%)

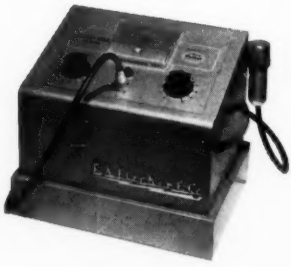
A MUST IN DERMATOLOGY

FISCHERQUARTZ

Model No. 88
Fischer Dry Pads For Low Volt
No Moisture * Send For Details

A MUST IN DEPENDABLE

ULTRA SOUND



RF-7 Ultra Sound with new 6 or 12 foot very thin, flexible low volt cables.

R. A. FISCHER & CO.
517-525 COMMERCIAL ST.
GLENDALE 3, CALIFORNIA
FISCHERTHERM • FISCHERSINE • FISCHERQUARTZ • FISCHER ULTRA SOUND

PRURITUS ANI

treated ORALLY with **Borcherdt's MALT SOUP EXTRACT (MALTSUPEX)** *shows good results*

We would like to send you the recently published paper by Dr. Louis H. Brooks who says, ***"It was found that administration of Malt Soup Extract in dosages of one or two tablespoonfuls twice daily produced favorable results. Within two or three days after beginning this simple regimen, the itching and burning usually disappeared. Frequently there was prompt remission of symptoms which was followed by improvement in the condition of the tissue of the anal canal and the perianal skin."****

What Malt Soup Extract is. It's a non-diastatic barley malt extract, neutralized with potassium carbonate.

How Malt Soup Extract works. It works by restoring the normal acid condition in the lower tract and by promoting the growth and development of aciduric bacteria.

How soon can results be expected? The itching and burning will usually disappear in about three days, while the healing of the perianal skin is usually complete in about three weeks.

What is the usual effective dose? Two tablespoonfuls, twice a day (heaping if powder) is the usual effective dose which can be reduced as symptoms disappear. (Allow for carbohydrate content when treating diabetics).

What forms are available? Two forms are to be found in most drug stores coast to coast—the original liquid and the newer, popular powder. Both are sold under the name: MALT SOUP EXTRACT (Maltsupex).

What sizes are to be had? Both powder and liquid come in 8 ounce and 16 ounce bottles.

**Diseases of the Colon & Rectum, Vol. 1, No. 5, Sept.-Oct. 1958*

Borcherdt Company

217 North Wolcott Avenue, Chicago 12, Illinois
In Canada, Chemo Drug Co., Ltd., Toronto, Canada

We will be glad to send you clinical samples of powder and (or) liquid.

Serving the Medical Profession
SINCE 1868

Borcherdt Company A
217 N. Wolcott Ave., Chicago 12, Ill.
Gentlemen: Please send me sample of Malt Soup Extract
☐ Powder ☐ Liquid and literature.

_____ M.D.

Address _____

City _____ Zone _____ State _____

No longer *itched*

bothered or

bewildered

Pruritus is relieved rapidly and erythema and lichenification of the skin are reduced within a short period after initial application of NEO-CORT-DOME. Secondary infection is controlled and the normal pH of the skin and external auditory canal is restored and maintained with NEO-CORT-DOME.

FOR INFECTIOUS DERMATOSES AND OTITIS EXTERNA

NEO-CORT-DOME™

CREME AND LOTION pH 4.6

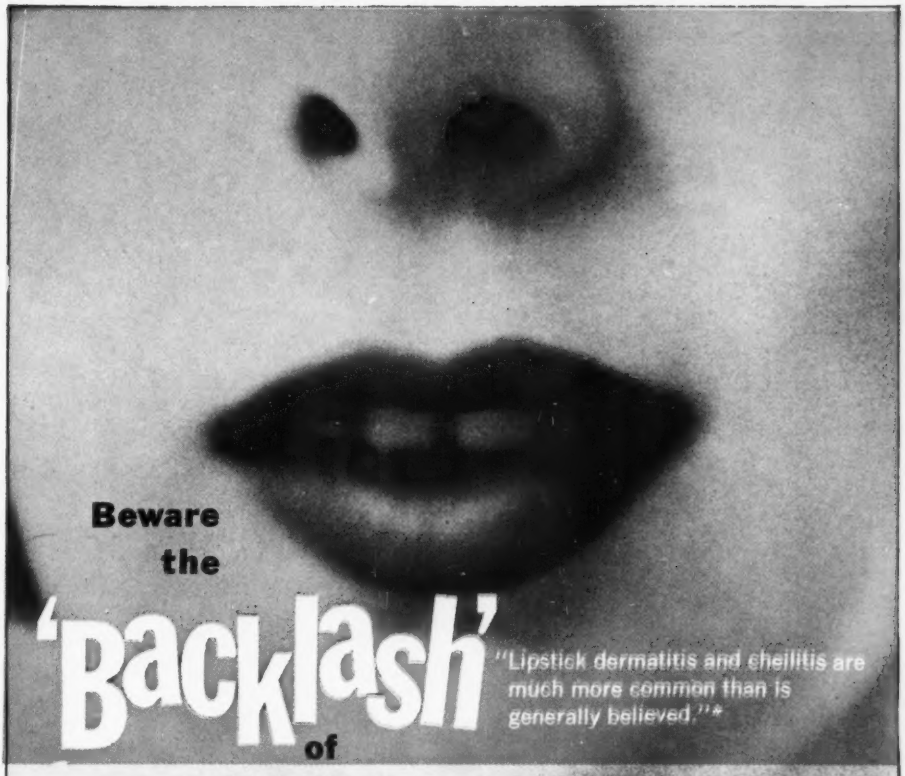
DOME

Hydrocortisone—Neomycin—In Aluminum Acetate Vehicle

Note: Lotion is especially effective in hairy areas and in tissue folds. *Supply:* ½% or 1% hydrocortisone, with 5 mg. per gm. Neomycin Sulfate in ½ oz., 1 oz., 4 oz. squeeze bottles. (½ oz. size has special soft plastic tip for easy application into external ear in otitis externa). *Sample* and literature available on request.

INCORPORATED IN EXCLUSIVE ACID MANTLE® VEHICLE

DOME CHEMICALS INC.
125 West End Avenue, New York 23
665 N. Robertson Blvd., Los Angeles 46
In Canada: 2675 Bates Road, Montreal



Beware the 'Backlash' of Beauty

"Lipstick dermatitis and cheilitis are much more common than is generally believed."*

Dermatoses resulting from sensitivity to a variety of lipstick ingredients can be avoided by using MARCELLE Lipsticks — another reason to remember and suggest MARCELLE® HYPOALLERGENIC COSMETICS for the patient with a cosmetic allergy or sensitivity.

MARCELLE Lipsticks — available in a full range of colors — are offered in different formulas to eliminate common sensitizers, and to avoid perfumes and the bromofluoresceins. The MARCELLE Lipstick Testing Kit, providing 14 different formulations, enables you to help your patient select a lipstick best suited to her case.

Marcelle COSMETICS

Borden's PHARMACEUTICAL DIVISION
350 Madison Avenue, New York 17

Available in Canada through Prof. Sales Corp., Montreal

*Zakon, S. J., et al.: Arch. Dermat. & Syph. 56:499, 1947; abstracted in Birmingham, D. J., and Campbell, P. C., Jr.: Occupational and Related Dermatoses, U. S. Public Health Service Publication No. 364, 1954.

A NEW WIDE-SPECTRUM TOPICAL MICROBICIDE

not an antibiotic... not a sulfonamide... not a nitrofuran

Triburon

& Triburon-HC

(containing hydrocortisone 0.5%)

EFFECTIVE EVEN AGAINST ANTIBIOTIC-RESISTANT STRAINS

HIGHLY ACTIVE

■ against most "pathogenic cocci [both staphylococci and streptococci] regardless of their resistance to antibiotics."[2]

■ against pathogens common in skin and wound infections.

VIRTUALLY NONSENSITIZING

■ in more than 4500 stringent, closed-patch sensitivity tests, the incidence of allergic response was less than 2 per cent.[2, 3]

■ in initial clinical studies, only 15 of 1014 patients developed evidence of skin irritation.

MINIMAL RESISTANT ORGANISMS

■ laboratory attempts to develop Triburon-resistant strains produced no substantial change in organism sensitivity.[3]

■ WIDE-SPECTRUM
■ RAPID-ACTING
■ WELL TOLERATED
■ NONSTAINING
■ ODORLESS

DIAGNOSIS AND NO. OF PATIENTS	DURATION OF TREATMENT	RESULTS	ADVERSE REACTIONS
Impetigo contagiosa (50)	Triburon 3-10 days	excellent	none
Ecthyma (24)	Triburon 5-14 days	excellent	none
Pustular folliculitis (16)	Triburon 1-3 weeks	infection controlled	3 complaints of burning
Dermatitis repens (18)	Triburon 1-2 weeks	infection controlled	none
Dermatitis repens (18)	Triburon-HC 1-4 weeks	excellent	none
Secondarily infected eczematous eruption (20)	Triburon 1-2 weeks	infection controlled	none
Secondarily infected eczematous eruption (64)	Triburon-HC 1-4 weeks	excellent	1 complaint of irritation

Chart based on finding of E. Edelson, E. Grunberg and T.V. Morton Jr.

PACKAGES:
Triburon Ointment, 1-oz tubes and 1-lb jars.
Triburon-HC Ointment, 5-Gm and 20-Gm tubes.

REFERENCES: 1. R. J. Schnitzer, E. Grunberg, W. F. DeLorenzo and R. E. Bagdon, to be published.
2. E. Edelson, E. Grunberg and T. V. Morton, Jr., Antibiotics Annual 1958-1959, New York, Medical Encyclopedia, Inc., 1959.
3. R. C. V. Robinson and L. E. Harmon, Antibiotics Annual 1958-1959.

TRIBURON™· triclobisonium chloride — N,N'-bis[1-methyl-3-(2,2,6-trimethylcyclohexyl) propyl]-N, -N'-dimethyl-1,6-hexanediamine bis (methochloride). ROCHE®

ROCHE LABORATORIES • Division of Hoffmann-La Roche Inc • Nutley 10 • New Jersey

Pleasingly and efficiently
serving patient and physician
during all seasons

SUPERFATTED

BASIS® SOAP

For dry sensitive skin
Available at Prescription Pharmacies

DUKE LABORATORIES, INC.
SOUTH NORWALK, CONN., U. S. A.

Mfrs. of Aquaphor®—Elastoplast®

"Doctor, will you tell me..."

What are the symptoms?
How shall I treat it?
What causes it?

For practical information about communicable disease, have your patients read:

SCARLET FEVER
8 pages, 15 cents

IMMUNIZATION
by Ruth A. Thomas, 8 pages, 15 cents

WHOOPING COUGH
by Constance Frick, 4 pages, 10 cents

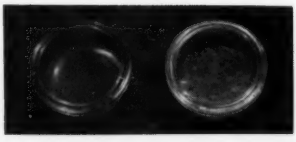
PNEUMONIA'S WATERLOO?
by William W. Bolton, 12 pages, 15 cents

WE CAN PREVENT DIPHTHERIA
by P. S. Rhoads, 8 pages, 15 cents

AMERICAN MEDICAL ASSOCIATION • 535 NORTH DEARBORN • CHICAGO 10

THE FUNGUS DIAGNOSTIC SERVICES

- **Prepared Plastic Plates for cultures**
- **Economical and easy to use (packages of 1 dozen)**
- **Samples on request**



Direct microscopic reports by return mail on skin specimens

7 Watchung Avenue
Plainfield, N. J.

ON THE SPOT TREATMENT

A TOPICAL FUNGICIDE FOR TOPICAL FUNGOUS INFECTIONS

Desenex attacks fungous infections caused by dermatophytes which affect the horny, keratinized layers of the skin.

Athlete's foot is a fungous infection of the skin involving the superficial layers that are not reached by the blood supply. A fungicidal agent, applied directly to these superficial fungous infections, brings the antifungal agent into intimate contact with the invading organism for a most effective method of treatment.

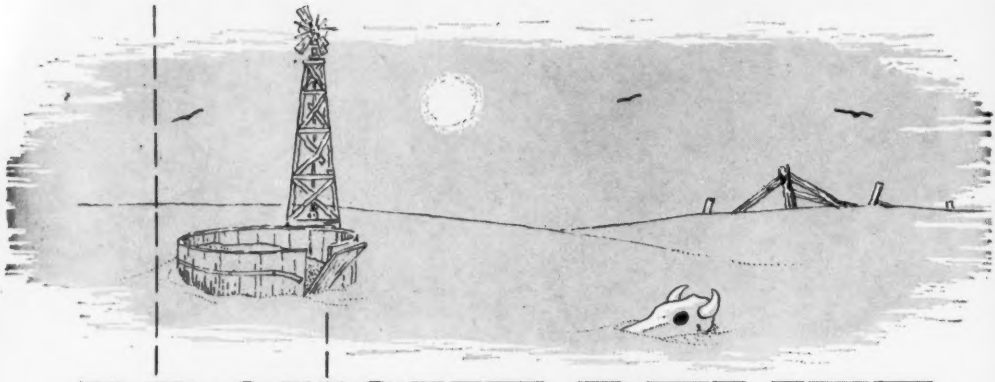
Desenex, a combination of zinc undecylenate and undecylenic acid – an unsaturated fatty acid with an 11-carbon chain – has resulted in a high percentage of "clinical" cures . . . proved to be among the least irritating, and best tolerated of all potent fungicidal agents.

ointment & solution & powder **DESENEX®** Maltbie

Maltbie Laboratories Division / Wallace & Tiernan Incorporated, Belleville 9, N. J.

PHOTOGRAPH, COURTESY DEPARTMENT OF DERMATOLOGY, UNIVERSITY OF PENNSYLVANIA

PD-96



DROUGHT RELIEF

for dry skin

LUBRIDERM*

topical application

Individuals suffering from parched, dry skin find immediate relief with soothing Lubriderm, a carefully balanced oil-in-water emulsion. As Lubriderm's aqueous outer-phase helps restore suppleness to drawn, taut skin, the oily inner-phase softens roughened, chapped areas and acts as a protective barrier to the further loss of moisture. When used persistently, Lubriderm insures a soft, smooth, comfortable skin condition.

*Contains cholesterol derivative of lanolin.

Lubath

bath additive

Many persons with dry skin experience bothersome itching and burning of the skin after bathing, a discomfort which generally worsens whenever the humidity of the air is low. Such after-bath pruritus is often controlled with the use of Lubath in the bath water. Lubath, a highly refined cottonseed oil made dispersible in hard or soft water by a non-irritating, non-ionic surfactant, deposits a thin film of oil over the entire body while bathing, usually bringing prompt relief.

IN CANADA—Omega Laboratories, Ltd., Montreal and Toronto
IN VENEZUELA—Salus, C. A. Caracas

For detailed information and samples, write . . .

TEXAS PHARMACAL COMPANY

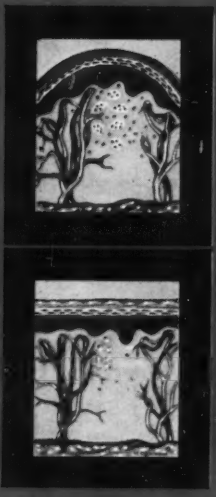
San Antonio, Texas

in acute dermatoses

as well as subacute and chronic skin diseases

"prompt remissions"[1]

"...when the tar-steroid cream TARCORTIN was prescribed for patients presenting very acute episodes of atopic dermatitis, contact dermatitis, psoriasis, chronic infectious eczematoid dermatitis, and other eczematous dermatoses...we were able to achieve prompt remissions..."[1]



1. Welsh, A. L., and Ede, M.: J.A.M.A. 160:156, 1956.

Additional Clinical Publications on Tarcortin:

Clyman, S. G.: Postgrad. Med. 21:309, 1957 • Bleiberg, J.: J. M. Soc. New Jersey 53:37, 1956 • Abrams, S. P., and Shaw, C.: Clin. Med. 3:839, 1956 • Bleiberg, J.: Am. Practitioner 8:1404, 1957

NEW TARCORTIN LOTION
excellent for lesions of head and hands
supplied—plastic squeeze bottles ½ ounce

TARCORTIN®

Cream — Hydrocortisone 0.5% and Special Coal Tar Extract 5% (TARBONISE) in a greaseless, stainless vanishing cream base. In tubes of 7 gm. and 1 oz.

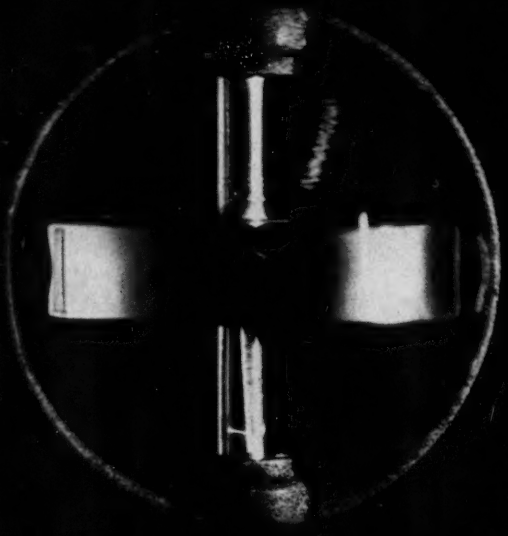
ALSO AVAILABLE: FOR DRY SCALY ECZEMAS, AND WHEN INFECTION IS PRESENT OR ANTICIPATED

NEO-TARCORTIN®

Ointment — Hydrocortisone 0.5%, Neomycin (as Sulphate) 0.35% and Special Coal Tar Extract 5%. In tubes of 7 gm. and 1 oz.

REED & CARNRICK Jersey City 6, New Jersey

minimal disturbance
of the patient's chemical and psychic balance...



still unsurpassed for total corticosteroid benefits

Aris

Substantiated by published reports of leading clinicians:

- **effective control** of allergic and inflammatory symptoms[1-20]
- **minimal disturbance** of the patient's chemical and psychic balance[1,4,5,8-19]

tocort®

Triamcinolone LEDERLE

At anti-inflammatory and antiallergic levels ARISTOCORT means:

- **freedom from salt and water retention**
- **virtual freedom from potassium depletion**
- **negligible calcium depletion**
- **euphoria and depression rare**
- **no voracious appetite — no excessive weight gain**
- **low incidence of peptic ulcer**
- **low incidence of osteoporosis with compression fracture**

Indications: rheumatoid arthritis; arthritis; respiratory allergies; allergic and inflammatory dermatoses; disseminated lupus erythematosus; nephrotic syndrome; lymphomas and leukemias.

Precautions: With ARISTOCORT all traditional precautions to corticosteroid therapy should be observed. Dosage should always be carefully adjusted to the smallest amount which will suppress symptoms. After patients have been on steroids for prolonged periods, discontinuance must be carried out gradually.

Supplied: Scored tablets of 1 mg. (yellow); 2 mg. (pink); 4 mg. (white); 16 mg. (white).

Diacetate Parenteral (for intra-articular and intrasynovial injection). Vials of 5 cc. (25 mg./cc.).

List of References 1-20 supplied on request.

Lederle LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, N. Y.

℞ For Household Hand Dermatitis

KNIT COTTON LINED

Bluettes®

Neoprene Rubber Gloves

Bluettes' knit cotton lining is permanently bonded to the liquidproof neoprene exterior, eliminating separate glove and liners. Regular hand or machine washing will not affect lining, bond or neoprene.

Patch Test Kits contain 1 centimeter diameter discs of Pioneer glove materials.

Mail Coupon For Patch Test Kits

The PIONEER Rubber Company
106 Tiffin Road, Willard, Ohio

Please send me:

- ☐ Patch Test Kit #7 — Household Glove Patch Test discs.
- ☐ Patch Test Kit #8 — Industrial Glove Patch Test discs.

NAME _____

ADDRESS _____

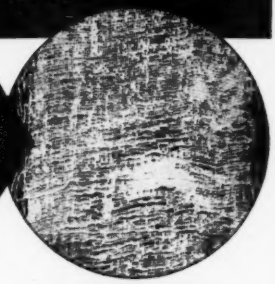
CITY _____ Zone ___ State _____

THE BEST IMPROVEMENT YET IN *UNNA'S BOOT*

NEW 4" x 10 YD.

Non-Ravelling DOME-PASTE® BANDAGE

DOME



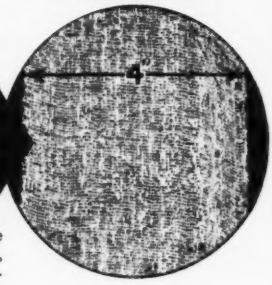
THE OLD

Frayed edges, uneven impregnation, difficult to apply.

•

Thread-locked edges, firmly woven; medicament spreads uniformly, easy to apply.

THE NEW



The new Dome-Paste bandage is flesh colored, 4" x 10 yd. gauze bandage . . . impregnated with glycerine, zinc oxide, gelatine paste.

RECOMMENDED

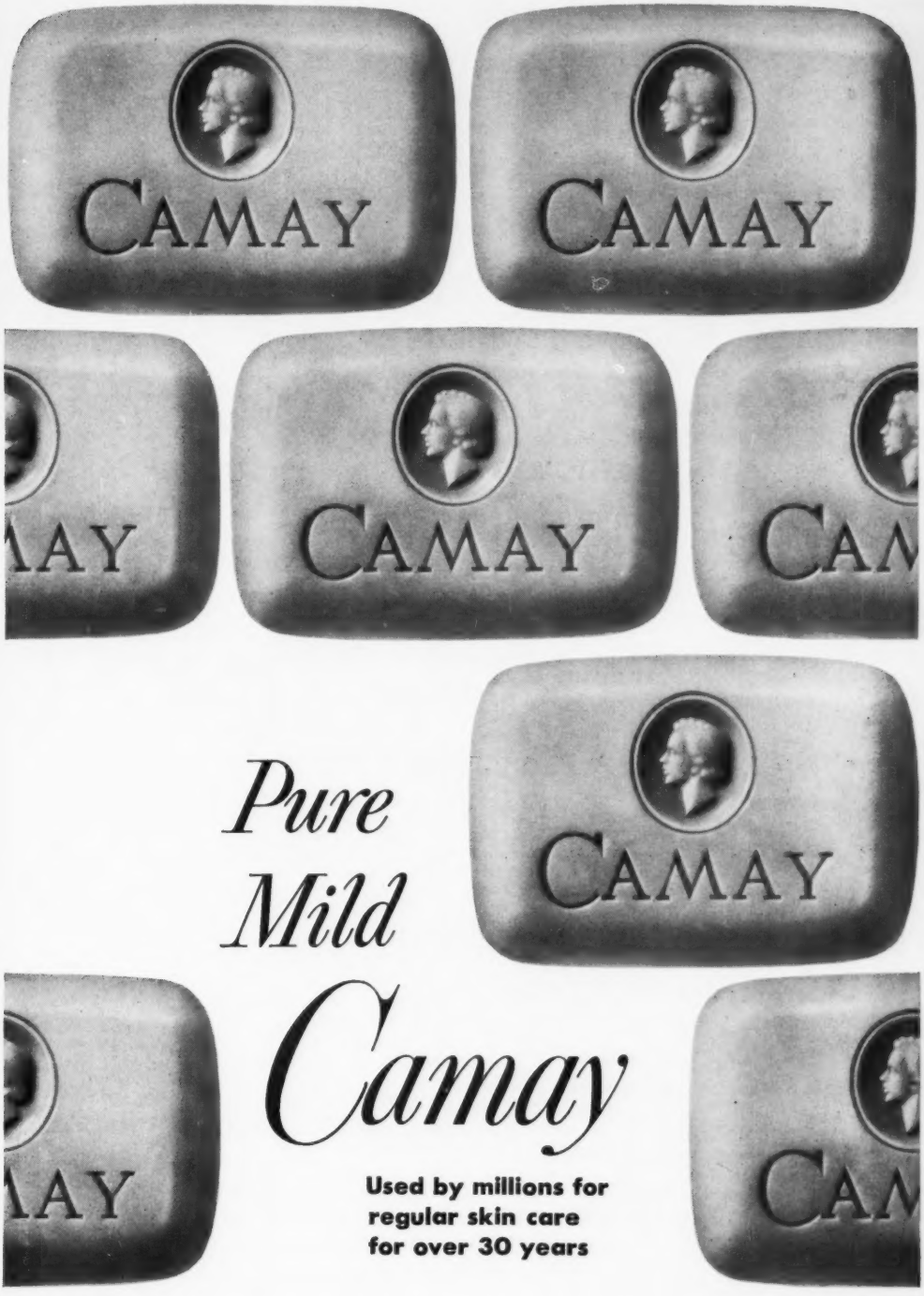
for leg ulcers resulting from thrombophlebitis (particularly the post partum and post-operative kinds), stasis edema and chronic venous insufficiency associated with varicose veins, and varicose eczema, lymphatic edema and thrombophlebitis of the superficial saphenous vessels.

AVAILABLE

Individually wrapped in sealed polyethylene bags, inserted in metal cans to insure freshness.

DOME CHEMICALS INC.

125 West End Avenue, New York 23, N. Y.
665 N. Robertson Blvd., Los Angeles 46, Cal.
2765 Bates Road, Montreal, Canada



©P&G Procter & Gamble

10 SPECIALTY JOURNALS

PUBLISHED MONTHLY
BY THE AMERICAN MEDICAL ASSOCIATION

NEUROLOGY

GENERAL PSYCHIATRY

SURGERY

PATHOLOGY

DISEASES OF CHILDREN

OPHTHALMOLOGY

INDUSTRIAL HEALTH

DERMATOLOGY

INTERNAL MEDICINE

OTOLARYNGOLOGY

Each journal offers the latest medical research and developments of outstanding specialists. Edited for the doctor by prominent authorities in each special field, these journals are of value not only to the specialist but to the general practitioner as well.

To order your subscription to one of the A.M.A.'s specialty journals use the form below.

AMERICAN MEDICAL ASSOCIATION
535 North Dearborn • Chicago 10

Please enter my subscription to the specialty journal checked at right.
Remittance for ☐ one year ☐ two years is enclosed.

NAME_____

ADDRESS_____

CITY_____ ZONE____ STATE_____

(One year rates)	U.S.A. & Possessions APO's	Canada	Outside U.S.A. & Possessions
☐ A.M.A. Arch. Neurology	$14.00	$14.50	$15.50
☐ A.M.A. Arch. Gen. Psychiatry	$14.00	$14.50	$15.50
☐ A.M.A. Arch. Dermatology	12.00	12.50	13.50
☐ A.M.A. Arch. Industrial Health	10.00	10.50	11.50
☐ A.M.A. Arch. Internal Medicine	10.00	10.50	11.50
☐ A.M.A. Jrl. Diseases of Children	12.00	12.50	13.50
☐ A.M.A. Arch. Surgery	14.00	14.50	15.50
☐ A.M.A. Arch. Pathology	10.00	10.50	11.50
☐ A.M.A. Arch. Ophthalmology	12.00	12.50	13.50
☐ A.M.A. Arch. Otolaryngology	14.00	14.50	15.50

A sense of
well being
for your
PSORIATIC
PATIENT

SOYALOID™

INDIVIDUAL DOME PACKETS

A colloid bath made with the exclusive
Soy Bean Colloid Fraction Component*
can produce a truly soothing, emollient effect—
and give the patient a feeling of well being.

A Colloid Bath with all these advantages: no stickiness—no fermentation odor—non-slippery—high in protein value (52% PROTEIN CONTENT)

Supply: Box of 5 packets, 3 oz. each

A most trusted name in Dermatologicals
DOME CHEMICALS INC.
125 WEST END AVENUE, NEW YORK 23
665 N. ROBERTSON BLVD., LOS ANGELES 46
2765 BATES ROAD, MONTREAL

*Pat. Pend'g

normal protective cover

Normal skin has an acid pH range between 4 and 6

Samples and literature on request

Supply:
ACID MANTLE Creme: 1 oz. tubes, 4 oz. & 16 oz. jars.
ACID MANTLE Lotion: 1 oz. and 4 oz. squeeze bottles, 1 pint bottles.

ACID MANTLE®

CREME or LOTION pH 4.2

In housewives' eczema and industrial dermatitis, promptly restores and maintains the normal protective acidity of the skin. Active ingredient is aluminum acetate in specially formulated bases.

"The importance of a measure designed to return the pH of the skin quickly to its normal values after exposure to soap and alkalies is amply borne out..."

—Gross, P., et al.: A. M. A. Arch. Dermat. & Syph. 70:94.1954.

DOME CHEMICALS INC.

125 West End Avenue, New York 23, N. Y.
665 N. Robertson Blvd., Los Angeles 46, Cal.
2765 Bates Road, Montreal, Canada

---

*TELES

Torch (available on prescription in 4 oz. bottles)

Really new, prompt and effective therapeutic agent in control of seborrheic dermatitis, itchy scalp and dandruff.

TELES • is a milk-white, unscented shampoo
TELES • may be employed at weekly intervals or less frequently
TELES • does not stain hair of any color
TELES • does not stimulate oiliness in the scalp
TELES • complete directions for use on each 4 oz. bottle

Samples and literature on request

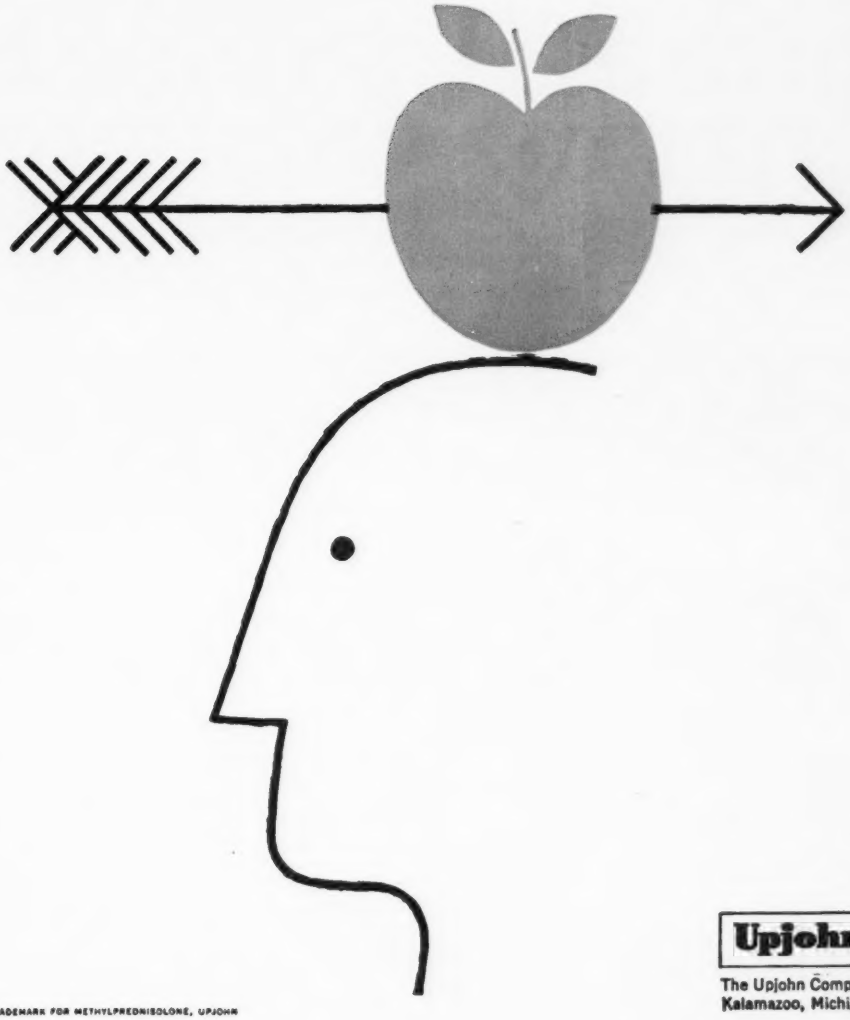
Reference: Gross E. R. and Wright C. S., A. M. A. Archives of Dermatology, 78:92, July, 1958

TORCH LABORATORIES, INC.

110 Chestnut Street • Philadelphia 6 • Pa. *Tellurium Dioxide Suspension, Torch

Medrol*

hits the disease but spares the patient



*TRADEMARK FOR METHYLPREDNISOLONE, UPJOHN

Upjohn

The Upjohn Company
Kalamazoo, Michigan

"ulcers were cleaned up promptly"*

"...previously treated unsuccessfully with antibiotic or antibacterial ointments...the ulcers were cleaned up promptly and complete healing was obtained....Necrotic tissue was effectively dissolved without injury to the viable tissues....Local infection was uniformly eradicated...."
Carter, C. H.: M. Times 86:1382 (Nov.) 1958.

panafil® topical enzyme therapy

Rystan
Mount Vernon, N.Y.

- effective wound cleansing and healing
- well tolerated and convenient for outpatient use
- economical for hospital and patient

PANAFIL ointment (papain – urea – water-soluble chlorophyll derivatives) • For complete information see your Physicians' Desk Reference 33359

NOW AVAILABLE

1958 EDITION

A.M.A. HEALTH PUBLICATIONS CATALOG

HEALTH PROBLEMS
MEDICAL CARE
MEDICAL EDUCATION AND HOSPITALS
MEDICAL ECONOMICS

SEND FOR YOUR FREE COPY

BUREAU OF HEALTH EDUCATION
AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET
CHICAGO 10, ILLINOIS

in urticaria and pruritus

VISTARIL* provides:

hydroxyzine pamoate

SPECIFIC ANTIHISTAMINIC EFFECT

in the treatment of a variety of skin disorders commonly seen in your practice.

"The most striking results were seen in those patients with chronic urticaria of undetermined etiology."[1]

. . . reduces—erythema, excoriation, and extent of lesions.[1-4]

PSYCHOTHERAPEUTIC POTENCY

for effective relief of tension and anxiety.[1-4]

Recommended Oral Dosage: 50 mg. q.i.d. initially; increase or decrease according to individual response.

Supplied as: Vistaril Capsules—25 mg., 50 mg. and 100 mg.

Vistaril Parenteral Solution—10 cc. vials and 2 cc. Steraject® Cartridges, each cc. contains 25 mg. hydroxyzine (as the HCl).

*Trademark

More than a tranquilizer

Pfizer *Science for the world's well-being*

PFIZER LABORATORIES
Division, Chas. Pfizer & Co., Inc.
Brooklyn 6, New York

References: 1. Feinberg, A. R., et al.: J. Allergy *29*:358 (July) 1958. 2. Eisenberg, B. C.: Clin. Med. *5*:897-904 (July) 1958. 3. Robinson, H. M., Jr., et al.: J.A.M.A. *161*:604-606 (June 16) 1956. 4. Robinson, H. M., Jr., et al.: South. M. J. *50*:1282 (Oct.) 1957.

for dramatic relief of penicillin reactions—
early treatment with

NEUTRAPEN®

(NEUTRALIZES PENICILLIN) (Penicillinase Injectable,* SchenLabs)

the only specific for penicillin reactions

"Penicillinase [Neutrapen] should be given as soon as possible after onset of symptoms."[5]
(M. C. Zimmerman – Antibiotics Annual, 1957-58)

- effective in 97% of cases[1]
- acts within an hour, lasts up to a week[2,3]
- one injection sufficient in 80% of cases[1]
- itching abates promptly[4]
- most reactions clear in 12 to 96 hours[1,5]
- well tolerated[1-9]
- may be lifesaving in certain anaphylactoid reactions[6,7]

Obscure sources—even cases with no history of penicillin therapy respond to NEUTRAPEN if the reaction has been caused by penicillin from sources such as milk, Roquefort or Bleu cheese, or penicillin-containing vaccines.[1,5,9]

NEUTRAPEN—800,000 units I. M.—should be given as soon as symptoms appear. May be repeated on the third day if response is not satisfactory. In anaphylactic reactions, epinephrine should be given and other supportive measures should be instituted immediately, followed by 800,000 units of NEUTRAPEN I. V. and 800,000 units I. M.

contraindications: None. *side effects:* Occasionally transient local soreness, erythema, and edema; rarely, transitory chills and fever. *supplied:* 800,000-unit, single-dose vials of lyophilized penicillinase powder. Stable at room temperature in the dry state.

References: (1) Zimmerman, M. C.: Clin. Med. *5*:305, 1958. (2) Becker, R. M.: New England J. Med. *254*:952, 1956. (3) Chen, J. Y. P.; Bard, J. W., and Balsito, A. A., in Welch, H., and Marti-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 321. (4) Minno, A. M., and Davis, G. M.: J.A.M.A. *165*:222 (Sept. 21), 1957. (5) Zimmerman, M. C., in Welch, H., and Marti-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 312. (6) Becker, R. M.: Ann. Int. Med. *48*:1228, 1958. (7) Becker, R. M., in Welch, H., and Marti-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 310. (8) Davis, G. M.: Discussion, Antibiotics Symposium, Washington, D. C., October 3, 1957. (9) Zimmerman, M. C.: J.A.M.A. *167*:1807 (Aug. 9), 1958.

®T. M. REG. U. S. PAT. OFF. *PATENTS PENDING 58059

SchenLabs SCHENLABS PHARMACEUTICALS, INC., NEW YORK 1, N. Y.

PSORIATICS

are half personalities, for an uncomfortable person is only one half a personality

EPIDOL®

will help to restore the psoriatics' appearance and self-confidence.

EPIDOL is a clear, *adhesive, non-greasy,* rapidly drying, improved Wright Liquor Carbonis Detergens plus Salicylic Acid 3%.

EASY to apply. Applicator comes with every bottle.

EASY to remove. Readily washes off with soap and water.

Discover how rapidly and effective EPIDOL may relieve the discomfort and clear the lesions. It helps restore the patient's feeling of comfort. Your psoriatic patients may, once again, become confident, full personalities.

SUPPLIED: Bottles with applicators: 3 fl. oz.—6 fl. oz.

Spirt & Co., Inc.
WATERBURY, CONN.

Samples, literature and reprints are available. Just write to:

KENACORT

SQUIBB TRIAMCINOLONE

for all your patients starting on corticoids

Kenacort provides these important advantages . . . excellent corticoid activity on a low dosage schedule[1-3] without edema,[1-4] psychic stimulation,[1-3] or adverse effect on blood pressure;[1-3,5] a low sodium diet is not necessary;[4,5] and gastrointestinal disturbances are usually negligible.[2,4,5] Because of these benefits, Kenacort starts all your patients off right — even your "problem" patients, such as the obese, the hypertensive, or the emotionally disturbed.

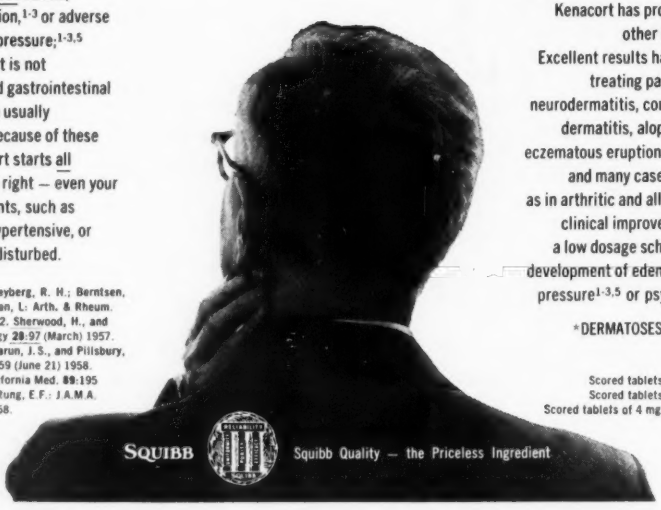
REFERENCES: • 1. Freyberg, R. H.; Berntsen, C. A., Jr., and Hellman, L: Arth. & Rheum. 1:215 (June) 1958. • 2. Sherwood, H., and Cooke, R. A.: J. Allergy 28:97 (March) 1957. • 3. Shelley, W. B.; Harun, J. S., and Pillsbury, D. M.: J.A.M.A. 167:959 (June 21) 1958. • 4. Dubois, E. L.: California Med. 89:195 (Sept.) 1958. • 5. Hartung, E. F.: J.A.M.A. 167:973 (June 21) 1958.

for all your patients with dermatoses* requiring corticoids

Kenacort quickly alleviates itching, erythema and irritation. Because of its enhanced antiallergic, anti-inflammatory and antipruritic activity, Kenacort has proved effective where other steroids have failed. Excellent results have been reported in treating patients with localized neurodermatitis, contact and seborrheic dermatitis, alopecia areata, chronic eczematous eruptions — including atopy, and many cases of psoriasis.[3] And, as in arthritic and allergic patients, rapid clinical improvement is obtained on a low dosage schedule[1-3] without the development of edema,[1-4] elevated blood pressure[1-3,5] or psychic stimulation.[1-3]

*DERMATOSES — a major indication

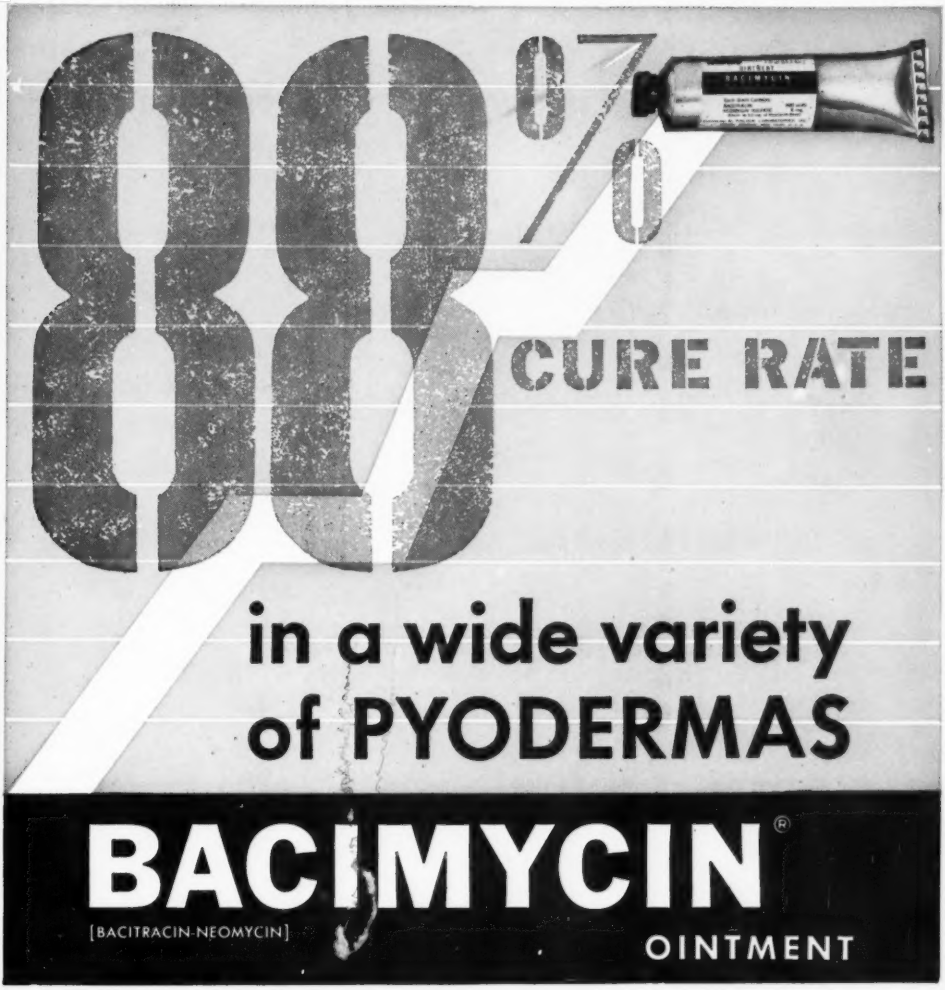
SUPPLIED:
Scored tablets of 1 mg. — Bottles of 50
Scored tablets of 2 mg. — Bottles of 50
Scored tablets of 4 mg. — Bottles of 30 and 100



SQUIBB

Squibb Quality — the Priceless Ingredient

"KENACORT" ® IS A SQUIBB TRADEMARK



a first choice for dual antibiotic therapy

In a recent study[1] of 53 patients with various types of pyodermas, the use of BACIMYCIN Ointment ". . . resulted in a cure rate of 88%. . . ." Impetigo, infectious eczematoid dermatitis, atopic eczema, secondary infections superimposed on dermatitis venenata, and folliculitis were among the common skin infections that showed marked improvement with BACIMYCIN therapy.

BACIMYCIN rarely produces sensitization or primary irritation.

Supplied in ½ oz. tubes for prescriptions; in 100 gm. jars for hospital use; in ⅛ oz. tubes for ophthalmic use. Also supplied as BACIMYCIN with Hydrocortisone, ⅛ oz. tube with applicator tip.

Literature and samples on request.

1. Greenhouse, J. M., and Ryle, W. C.: A.M.A. Arch. Dermat. & Syph. 69:366 (March) 1954.

Walker **LABORATORIES, INC.** MOUNT VERNON, NEW YORK

CULTURE MEDIA AVAILABLE

Mycosel Agar

Sabouraud's Dextrose Agar

Sabouraud's Maltose Agar

Corn Meal Agar

Potato Dextrose Agar

Sabouraud's Dextrose with Penicillin

Sabouraud's Dextrose with Streptomycin

Chlamydospore Agar

Littman's Oxgall Agar

"It is considerably cheaper to use these bottles once and discard them than to pay the labor cost of reconditioning an equal number of test tubes."

...*Practical Medical Mycology*
By J. Walter Wilson, M.D. and Orda A. Plunkett, Ph.D.
Arch D & S 59:414, April 1949

A PREFERRED METHOD for the CULTURE of FUNGI as an OFFICE PROCEDURE

WRITE FOR INFORMATIVE LITERATURE

DERM MEDICAL Sterile Glass Containers holding Sabouraud's Dextrose Agar offer a simple, accurate method for the culture of fungi pathogenic to man. When indicated for diagnosis and study of mycotic diseases, can be used as a routine office procedure. For institutional use, this method has proved both efficient and economical.

Derm Medical

Manufacturers of Culture Media in Sterile Containers

DM 3

DEPT. "D", P. O. BOX 78595 • WEST ADAMS STATION • LOS ANGELES 16, CALIF.